7-1-2021

The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer

Alexander B Olawaiye
University of Pittsburgh

Thomas P Baker
Defense Health Agency National Capital Regional Medical Directorate

M Kay Washington
Vanderbilt University

David G Mutch
Washington University School of Medicine in St. Louis

The New (Version 9) American Joint Committee on Cancer Tumor, Node, Metastasis Staging for Cervical Cancer

Alexander B. Olawaiye, MD [1]; Thomas P. Baker, MD[2]; M. Kay Washington, MD, PhD[3]; David G. Mutch, MD[4]

[1]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh School of Medicine, Magee-Women's Hospital of the University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; [2]The Joint Pathology Center, Defense Health Agency National Capital Regional Medical Directorate, Silver Spring, Maryland; [3]Department of Pathology, Vanderbilt University Medical Center, Nashville, Tennessee; [4]Department of Obstetrics and Gynecology, Washington University School of Medicine, St Louis, Missouri.

Corresponding Author: Alexander B. Olawaiye, MD, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh School of Medicine, Magee-Women's Hospital of UPMC, 300 Halket Street, Pittsburgh, PA 15213 (olawaiyea@mail.magee.edu).

DISCLOSURES: The authors report no conflicts of interest.

Thomas P. Baker's contributions to this article are his views and do not reflect the official policy of the Departments of the Army, Navy, or Air Force; the Department of Defense; or the US government.

doi: 10.3322/caac.21663. Available online at cacancerjournal.com

Abstract: The American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) staging for all cancer sites has been periodically updated as a published manual for many years. The last update, the eighth edition *AJCC Cancer Staging Manual* went into use on January 1, 2018. The AJCC has since restructured and updated its processes, and all AJCC staging-related data are now housed on its new application programming interface. Consequently, the next AJCC TNM staging update, AJCC version 9 TNM staging, will be published electronically and will be released chapter by chapter. The first chapter of version 9 AJCC TNM staging is the updated cervical cancer staging, which is now published. This article highlights the changes to the AJCC TNM cervical cancer staging; these changes align with the International Federation of Gynecology and Obstetrics staging. The most important of the changes are: 1) the incorporation of imaging and surgical findings, 2) the elimination of lateral spread from T1a, 3) the addition of a subcategory to T1b (T1b3), and 4) histopathology is updated to reflect human papillomavirus-associated and human papillomavirus-independent carcinomas. **CA Cancer J Clin 2021;71:287-298.**

Keywords: American Joint Committee on Cancer (AJCC), version 9, staging, cervix

Introduction

Cervical cancer remains a worldwide pandemic. In 2018, there were an estimated 570,000 new cases and 311,000 deaths worldwide, making it the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women. In low human development index (HDI) settings, cervical cancer ranks second to breast cancer in incidence and mortality among women. It is the most commonly diagnosed cancer for women in 28 countries and the leading cause of cancer death in 48 countries; these countries are mostly located in sub-Saharan Africa and South-Eastern Asia.[1]

In countries with well established screening programs, the burden of cervical cancer is comparatively less. For instance, age-standardized incidence rates are lowest in Western Asia and Australia/New Zealand (4.1 and 6.0 cases annually per 100,000 women, respectively) and highest in Southern Africa and Eastern Africa (43.1 and 40.1 cases annually per 100,000 women, respectively). Similarly, mortality rates vary from 1.7 and 1.9 deaths annually per 100,000 women in Australia/New Zealand and Northern America, respectively, to 30.0 and 23.0 deaths annually per 100,000 women in Eastern Africa and Western Africa, respectively.[1] The United States estimates for 2020 are 13,800 new cases and 4290 deaths.[2] To facilitate research and progress in the treatment of cervical cancer, it is critical that disease spread description is uniform and

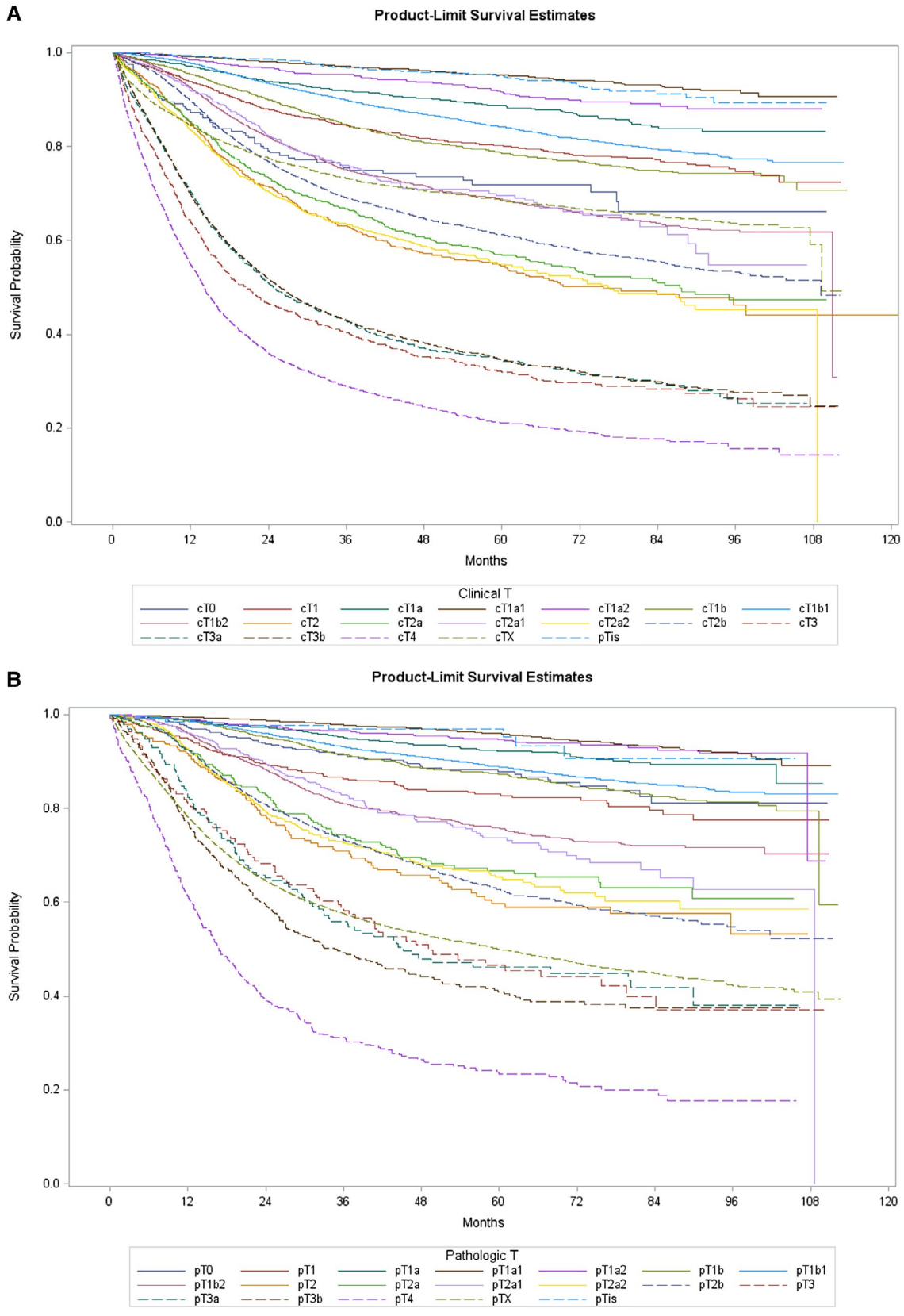

FIGURE 1. (A,B) Overall Survival Estimates by Tumor (T) Category. cT indicates clinical T category; pT, pathologic clinical category; pTis, pathologic tumor in situ.

is guided by the same rules across national and internal borders, which is the main purpose of staging.

Staging Systems for Gynecologic Cancers

There are 2 staging systems for gynecologic cancers used by clinicians for evaluating prognosis and choosing among treatment options, the tumor, node, metastasis (TNM) system and the International Federation of Obstetrics and Gynecology (FIGO) system. The TNM system is produced by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC). The AJCC liaises with both the FIGO and the UICC in producing its TNM staging. As a result of this collaboration, the AJCC TNM staging aligns with FIGO staging, the only difference being that the AJCC TNM staging includes granular details of each staging component. Also, there is no regularity to the frequency of staging updates by FIGO, whereas AJCC staging updates have been published on average every 5 or 6 years for the last 4 decades.

The Oncology Committee of FIGO published its most recent update to cervical cancer staging in 2019,[3] exactly a year after the AJCC eighth edition staging manual went into effect. Therefore, it was not feasible for the AJCC to include cervical staging update in its eighth edition staging manual. In addition, over the past 2 years, the AJCC has engaged in major reorganization and retuning; for instance, it has developed an application programming interface, reconstituted its editorial board, and redefined how AJCC TNM staging updates are going to be done and published going forward. The new version 9 AJCC TNM cervical cancer staging update offers the first glimpse into the new AJCC approach to guiding and ensuring the fidelity of staging.[4]

Compared with the AJCC eighth edition of cervical cancer TNM staging, the version 9 AJCC TNM cervical cancer staging update includes many changes, which represent a radical departure from all earlier versions of cervical cancer TNM staging. Overall, the new version 9 AJCC TNM cervical cancer staging allows for all the factors considered in management planning to be reflected in staging. This is really important because the AJCC eighth edition cervical cancer TNM staging is based on information acquired by clinical examination and very basic imaging and thus is

TABLE 1. Tumor (T) Category

T CATEGORY	FIGO STAGE	T CRITERIA
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded)
T1a	IA	Invasive carcinoma that can be diagnosed only by microscopy with maximum depth of invasion ≤5 mm
T1a1	IA1	Measured stromal invasion ≤3 mm in depth
T1a2	IA2	Measured stromal invasion >3 mm and ≤5 mm in depth
T1b	IB	Invasive carcinoma with measured deepest invasion >5 mm (greater than stage IA); lesion limited to the cervix uteri with size measured by maximum tumor diameter; note: the involvement of vascular/lymphatic spaces should not change the staging, and the lateral extent of the lesion is no longer considered
T1b1	IB1	Invasive carcinoma >5 mm depth of stromal invasion and ≤2 cm in greatest dimension
T1b2	IB2	Invasive carcinoma >2 cm and ≤4 cm in greatest dimension
T1b3	IB3	Invasive carcinoma >4 cm in greatest dimension
T2	II	Carcinoma invades beyond the uterus but has not extended onto the lower one-third of the vagina or to the pelvic wall
T2a	IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
T2a1	IIA1	Invasive carcinoma ≤4 cm in greatest dimension
T2a2	IIA2	Invasive carcinoma >4 cm in greatest dimension
T2b	IIB	With parametrial invasion but not up to the pelvic wall
T3	III	Carcinoma involves the lower one-third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney; note: the pelvic wall is defined as the muscle, fascia, neurovascular structures, and skeletal portions of the bony pelvis; cases with no cancer-free space between the tumor and pelvic wall by rectal examination are FIGO stage III
T3a	IIIA	Carcinoma involves the lower one-third of the vagina, with no extension to the pelvic wall
T3b	IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
T4	IVA	Carcinoma has involved (biopsy-proven) the mucosa of the bladder or rectum or has spread to adjacent organs (bullous edema, as such, does not permit a case to be assigned to stage IVA)

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 2. Clinical Tumor (cT) Category: Number of Patients at Risk (Corresponds to cT Kaplan-Meier Graph)

	MONTHS										
cT CATEGORY	0	12	24	36	48	60	72	84	96	108	120
cT0	245	201	165	133	105	75	50	23	8	1	0
cT1	3958	3379	2722	2156	1649	1187	757	405	152	9	0
cT1a	1855	1618	1360	1107	858	633	418	239	88	5	0
cT1a1	4484	3986	3253	2592	1964	1388	900	545	195	14	0
cT1a2	1433	1275	1039	822	621	457	297	176	69	4	0
cT1b	3353	3004	2500	1993	1527	1166	810	466	208	16	0
cT1b1	11,483	10,274	8256	6448	4841	3430	2159	1200	435	28	0
cT1b2	6200	5249	3893	2861	2139	1464	915	500	181	13	0
cT2	904	725	542	410	304	205	129	69	28	2	1
cT2a	1441	1145	841	653	467	328	207	95	36	3	0
cT2a1	797	674	475	337	230	150	83	39	11	0	
cT2a2	1855	1398	934	631	436	265	151	70	22	1	0
cT2b	10,760	8875	6301	4528	3236	2234	1383	730	271	22	0
cT3	1128	651	384	288	193	131	84	46	19	3	0
cT3a	1883	1198	724	482	299	209	136	76	23	0	
cT3b	8670	5543	3437	2317	1548	1043	629	333	117	11	0
cT4	3611	1775	931	581	386	243	145	72	26	3	0
cTX	9392	7006	5309	4026	3002	2075	1279	712	272	14	0
pTis	1613	1443	1186	913	679	482	296	163	56	1	0

Abbreviation: pTis, pathologic tumor in situ.
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 3. Pathologic Tumor Category (pT): Number of Patients at Risk (Corresponds to pT Kaplan-Meier Graph)

	MONTHS										
pT CATEGORY	0	12	24	36	48	60	72	84	96	108	120
pT0	732	642	512	394	266	181	112	59	24	2	0
pT1	719	628	510	408	308	224	159	98	39	1	0
pT1a	1765	1585	1334	1087	841	620	412	223	82	6	0
pT1a1	6959	6165	5006	3887	2917	2010	1264	695	244	12	0
pT1a2	2213	1975	1596	1252	924	659	416	205	74	3	0
pT1b	3128	2866	2383	1919	1514	1143	763	438	183	14	0
pT1b1	13,064	11,786	9510	7375	5501	3877	2419	1327	487	34	0
pT1b2	2704	2388	1853	1411	1114	803	513	291	110	8	0
pT2	299	263	199	149	116	76	53	31	12	0	
pT2a	410	357	278	209	161	109	70	38	14	0	
pT2a1	626	563	419	310	227	138	88	40	15	1	0
pT2a2	734	619	428	323	233	146	88	46	20	0	
pT2b	2442	2119	1607	1211	892	594	375	205	82	8	0
pT3	200	149	107	81	53	38	27	14	6	2	0
pT3a	234	173	115	88	58	44	33	20	6	0	
pT3b	598	434	301	219	152	109	66	38	16	0	
pT4	516	294	161	107	76	52	31	18	7	0	
pTX	16,606	12,070	9003	6981	5207	3690	2325	1282	470	32	0
pTis	143	132	125	110	80	57	30	16	10	0	

Abbreviation: pTis, pathologic tumor in situ.
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 4. Lymph Node (N) Category

N CATEGORY[a]	FIGO STAGE	N CRITERIA
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) ≤0.2 mm or single cells or clusters of cells ≤200 cells in a single lymph node cross-section
N1	IIIC1	Regional lymph node metastasis to pelvic lymph nodes only
N1mi	IIIC1	Regional lymph node metastasis (>0.2 mm but ≤2.0 mm in greatest dimension) to pelvic lymph nodes
N1a	IIIC1	Regional lymph node metastasis (>2.0 mm in greatest dimension) to pelvic lymph nodes
N2	IIIC2	Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2mi	IIIC2	Regional lymph node metastasis (>0.2 mm but ≤2.0 mm in greatest dimension) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	IIIC2	Regional lymph node metastasis (>2.0 mm in greatest dimension) to para-aortic lymph nodes, with or without positive pelvic lymph nodes

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.
[a]The suffix (f) is added to the N category when metastasis is identified only by fine-needle aspiration or core biopsy. The suffix (sn) is added to the N category when metastasis is identified only by sentinel lymph node biopsy.
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 5. Clinical Lymph Node (cN) Category: Number of Patients at Risk (Corresponds to cN Kaplan-Meier Graph)

	MONTHS										
cN CATEGORY	0	12	24	36	48	60	72	84	96	108	120
cN0	53,352	44,836	34,557	26,264	19,434	13,706	8610	4724	1751	119	1
cN1	16,739	11,104	6925	4666	3151	2037	1259	664	226	17	0
cNX	6124	4384	3445	2820	2185	1597	1059	615	247	14	0

SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 6. Pathologic Lymph Node (pN) Category: Number of Patients at Risk (Corresponds to pN Kaplan-Meier Graph)

	MONTHS										
pN CATEGORY	0	12	24	36	48	60	72	84	96	108	120
cN0	1837	1398	687	132	34	17	9	6	3	0	
pN0	23,884	21,330	17,463	13,982	10,681	7661	4906	2703	1023	57	0
pN1	5628	4852	3672	2723	2025	1371	872	484	178	19	0
pNX	21,553	16,498	12,608	9847	7319	5142	3222	1762	653	47	0

Abbreviation: cN, clinical lymph node category.
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

practically irrelevant to management planning. The purpose of this article is to provide a high-level overview of the major changes in the version 9 AJCC TNM cervical cancer staging update.

General Changes

All modalities of imaging are now allowed to be used for staging. This is perhaps the most important change because previous versions of cervical cancer staging only allowed plain radiographs, including intravenous pyelography, to be used for staging. With version 9, findings from ultrasound and cross-sectional imaging, such as computerized tomography, magnetic resonance imaging, and positron emission tomography, are all allowed to be incorporated into staging.

Another critical change is the incorporation of pathologic findings into staging. AJCC version 9 TNM staging for cervical cancer better defines how pathologic findings from examination of biopsy, excision, or surgical resection specimens can be used to determine clinical and

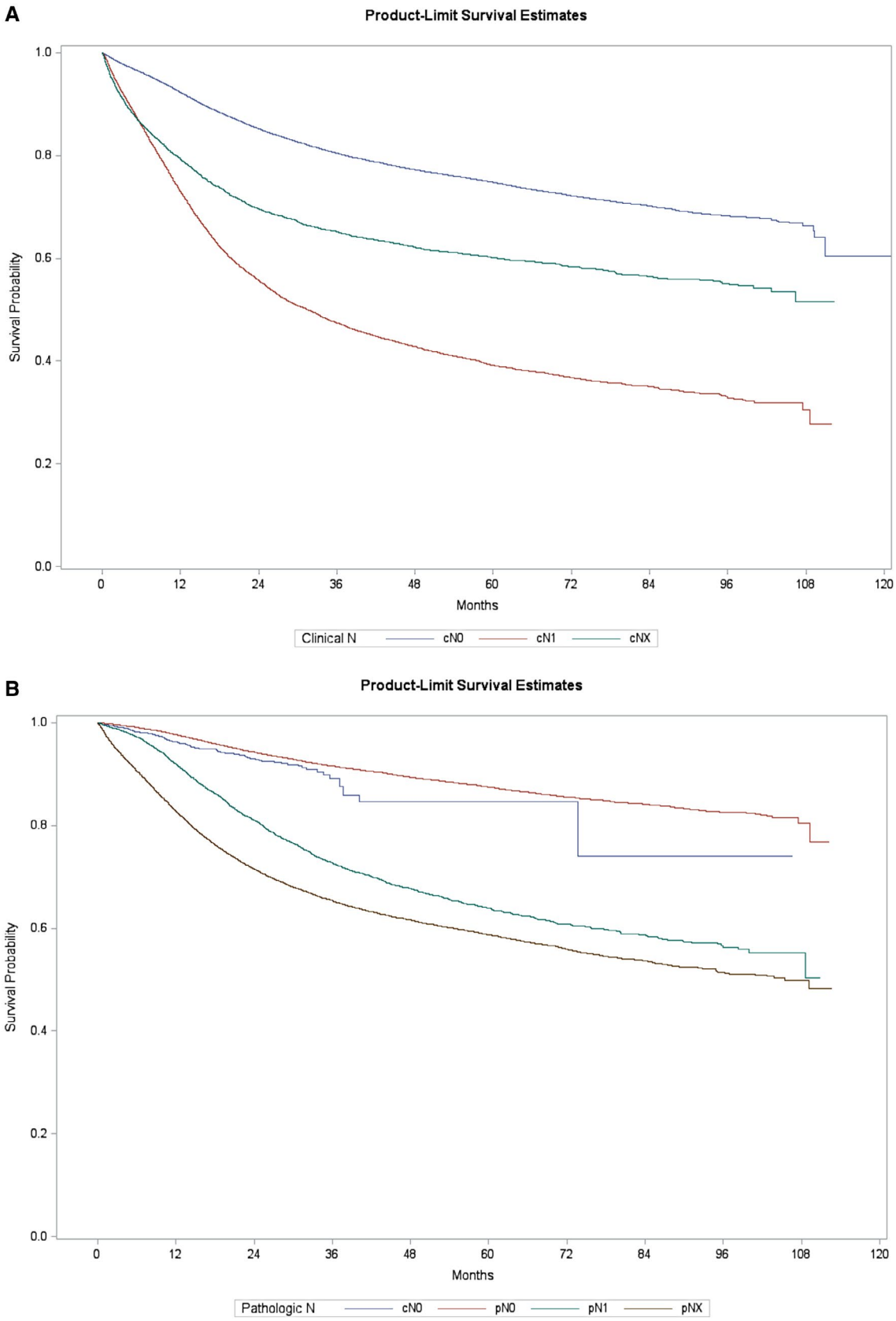

FIGURE 2. (A,B) Overall Survival Estimates by Lymph Node (N) Category. cN indicates clinical N category; pN, pathologic N category.

TABLE 7. Metastasis (M) Category

M CATEGORY	FIGO STAGE	M CRITERIA
M0		No distant metastasis
cM1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone; excludes metastasis to pelvic or para-aortic lymph nodes or vagina)
pM1	IVB	Microscopic confirmation of distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone; excludes metastasis to pelvic or para-aortic lymph nodes or vagina)

Abbreviations: cM, clinical metastasis category; FIGO, International Federation of Gynecology and Obstetrics; pM, pathologic metastasis category.
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 8. Clinical Metastasis (cM) Category: Number of Patients at Risk (Corresponds to cM Kaplan-Meier Graph)

	MONTHS										
cM Category	0	12	24	36	48	60	72	84	96	108	120
cM0	64,470	53,964	40,917	30,769	22,632	15,860	10,006	5494	2040	140	1
cM1	8725	3894	1983	1235	732	444	239	115	38	4	0
cMX	2	2	1	1	1	1	1	1	0		
pM1	444	203	51	10	2	1	0				

Abbreviation: pM, pathologic metastasis category
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 9. Pathologic Metastasis (pM) Category: Number of Patients at Risk (Corresponds to Pathologic pM Kaplan-Meier Graph)

	MONTHS										
pM CATEGORY	0	12	24	36	48	60	72	84	96	108	120
cM0	10,757	8324	3576	521	124	72	54	39	16	1	0
cM1	412	201	62	14	3	2	0				
pM0	18	15	15	9	7	6	4	3	2	0	
pM1	2312	1243	700	442	278	182	95	47	22	2	0

Abbreviation: cM, clinical metastasis category
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

pathologic stage. For example, tumor measurement from a radical hysterectomy specimen is used to determine the pathologic tumor category and takes priority over measurements from either clinical examination or cross-sectional imaging.

AJCC version 9 TNM staging for cervical cancer also include a concise workup table that lists diagnostic workup done, a description of reasons for the workup, and the specific contribution of each test or procedure to TNM category.

The AJCC version 9 TNM cervical cancer staging has the most current histology list from the World Health Organization Classification of Tumor series.[5] Finally, the histopathology list has been updated to include human papillomavirus (HPV)-associated and HPV-independent carcinomas. The HPV status of the cancer is indirectly determined by p16 immunohistochemical overexpression, which is considered a good surrogate marker of HPV-associated tumors. The need for this specific update, which does not affect the TNM categories, is that HPV-associated cervical cancer has a more favorable prognosis than HPV-independent cervical cancer.[6-8] Approximately 10% of cervical carcinomas are HPV-negative.[6,7] In one study, patients who had HPV-negative tumors were older, had more advanced disease at diagnosis, and were more frequently diagnosed with nonsquamous histology; moreover, they had a significantly worse disease-free survival (60 months vs 132 months) and overall survival (77 months vs 154 months) compared with women who had HPV-positive tumors.[7]

T Category Changes

T1a, which previously depended on both the extent of horizontal spread and the depth of disease invasion, is

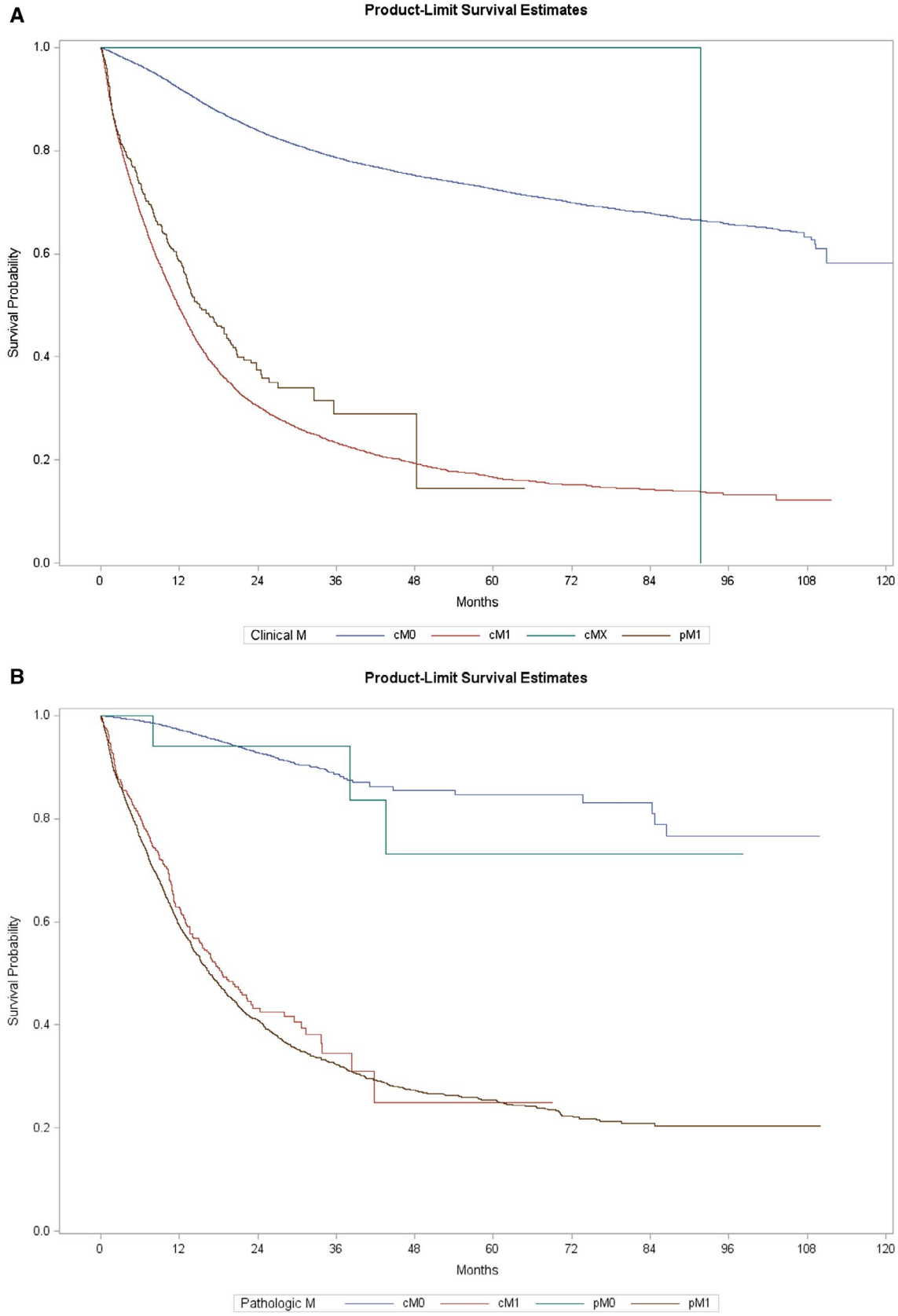

FIGURE 3. (A,B) Overall Survival Estimates by Metastasis (M) Category. cM indicates clinical M category; pM, pathologic M category.

TABLE 10. American Joint Commission on Cancer Prognostic Stage Groups

WHEN T IS…	AND N IS…	AND M IS…	THEN THE STAGE GROUP IS…
T1	N0	M0	I
T1a	N0	M0	IA
T1a1	N0	M0	IA1
T1a2	N0	M0	IA2
T1b	N0	M0	IB
T1b1	N0	M0	IB1
T1b2	N0	M0	IB2
T1b3	N0	M0	IB3
T2	N0	M0	II
T2a	N0	M0	IIA
T2a1	N0	M0	IIA1
T2a2	N0	M0	IIA2
T2b	N0	M0	IIB
T3	N0	M0	III
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
TX, T0, T1-T3	N1	M0	IIIC1
TX, T0, T1-T3	N2	M0	IIIC2
T4	Any N	M0	IVA
Any T	Any N	M1	IVB

Abbreviations: M, metastasis category; N, lymph node category; T, tumor category;
SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 11. Number of Patients at Risk for Clinical Stage Group Diagnosed From 2010 to 2017

CLINICAL STAGE GROUP	MONTHS										
	0	12	24	36	48	60	72	84	96	108	120
I	3054	2798	2470	2022	1609	1226	857	547	288	115	7
IA	1522	1380	1255	1066	861	648	457	305	171	55	4
IA1	4031	3772	3327	2726	2146	1607	1096	739	412	141	11
IA2	1236	1162	1013	839	668	502	378	258	139	52	3
IB	2483	2338	2093	1746	1417	1118	842	580	349	131	5
IB1	9331	8776	7751	6251	4802	3573	2488	1607	877	284	16
IB2	4114	3753	3148	2434	1861	1378	911	585	299	90	4
II	430	374	311	249	194	143	97	73	42	11	1
IIA	861	761	629	485	361	275	183	113	52	16	0
IIA1	538	494	414	306	219	151	99	54	26	5	0
IIA2	954	840	682	472	337	215	141	85	48	9	0
IIB	6442	5762	4657	3509	2637	1937	1313	831	450	170	7
III	258	173	128	96	73	49	37	23	11	6	1
IIIA	684	520	367	260	181	123	82	58	31	7	0
IIIB	3444	2574	1876	1361	988	717	468	301	151	59	4
IIIC1	9086	7453	5487	3965	2839	1970	1316	820	435	137	7
IVA	1793	1102	713	465	314	207	137	87	45	13	2
IVB	8640	4075	2261	1415	910	577	348	199	104	33	2

SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

TABLE 12. Number of Patients at Risk for Pathologic Stage Group Diagnosed From 2010 to 2017

PATHOLOGIC STAGE GROUP	MONTHS										
	0	12	24	36	48	60	72	84	96	108	120
I	99	91	60	30	5	1	1	1	1	1	0
IA	208	192	152	76	19	5	3	3	3	0	
IA1	1209	1101	822	361	51	8	6	5	4	2	1
IA2	507	467	338	124	11	2	2	2	2	1	0
IB	460	424	316	133	24	10	8	8	6	3	1
IB1	2841	2616	1948	805	93	22	12	8	5	3	0
IB2	402	369	253	91	7	4	2	0			
II	28	26	17	6	2	0					
IIA	29	27	24	8	2	1	1	1	0		
IIA1	100	96	70	26	3	0					
IIA2	99	89	57	20	3	0					
IIB	238	223	165	67	11	6	4	1	0		
III	9	9	6	5	1	1	0				
IIIA	18	15	11	8	3	0					
IIIB	25	19	10	2	1	0					
IIIC1	992	921	668	269	44	13	4	4	1	0	
IVA	57	40	20	7	3	2	1	1	0		
IVB	2500	1431	884	532	341	228	136	84	43	13	0

SOURCE: Used with permission of the American College of Surgeons, Chicago, Illinois.

now solely based on depth of invasion. Unlike the depth of invasion, extent of lateral spread is considered to be a less accurate measurement,[9] it can be recorded but would not count toward staging. Along the same lines, designating a microscopic disease as T1b is also based on a depth of invasion >5 mm.

T1b has been divided into 3 subcategories, T1b1, T1b2, and T1b3, based on size (maximum diameter), which are ≤2 cm, >2 to ≤ 4 cm, and >4 cm, respectively. This division was informed by the consistent contribution of tumor size to prognosis.[10-12]

There is no update to the T2, T3 and T4 categories except that information from cross-sectional imaging can now be used to determine these categories and, where surgical resection has been done, the findings from specimen examination are used for pathologic staging. A complete description of the T category is provided in Table 1. Survival estimates by clinical and pathologic T categories using National Cancer Database (NCDB) data (2010-2017) are depicted in Figure 1A,B, with the corresponding number of patients at risk shown in Tables 2 and 3.

N Category Changes

Lymph node involvement has a negative impact on the prognosis of cervical cancer.[13,14] Para-aortic lymph node involvement portends a worse prognosis than pelvic lymph node involvement,[15,16] yet all previous versions of cervical cancer staging did not allow the incorporation of lymph node status. This made these earlier versions irrelevant to primary surgical/radiotherapy or adjuvant management planning because lymph node involvement is critically considered in all treatment scenarios. The AJCC version 9 cervical cancer TNM staging update incorporates lymph node status in the N category. Again, the status is allowed to be determined by radiologic and surgical findings. Surgical methods of detection include fine-needle aspiration, core-needle biopsy, excisional biopsy, or lymphadenectomy.

When a lymph node (or lymph nodes) is available for pathologic assessment, involved lymph nodes fall into 1 of 3 categories based on the size of the metastases; 1) individual tumor cells (ITCs) <0.2 mm, 2) micrometastasis from 0.2 to 2 mm, and 3) macrometastasis >2 mm. In alignment with FIGO, only micrometastasis and macrometastasis count as positive lymph node involvement.[17] ITCs are to be recorded as pathologic N0(i+) but would have no impact on the N category of the AJCC version 9 cervical cancer TNM staging. This is considered important because the data may be used to guide future staging updates.

Pelvic lymph node involvement is designated N1, and para-aortic lymph node involvement is designated N2 (Table 4). Survival estimates by clinical and pathologic N categories using NCDB data (2010-2017) are depicted in Figure 2A,B, with the corresponding number of patients at risk shown in Tables 5 and 6.

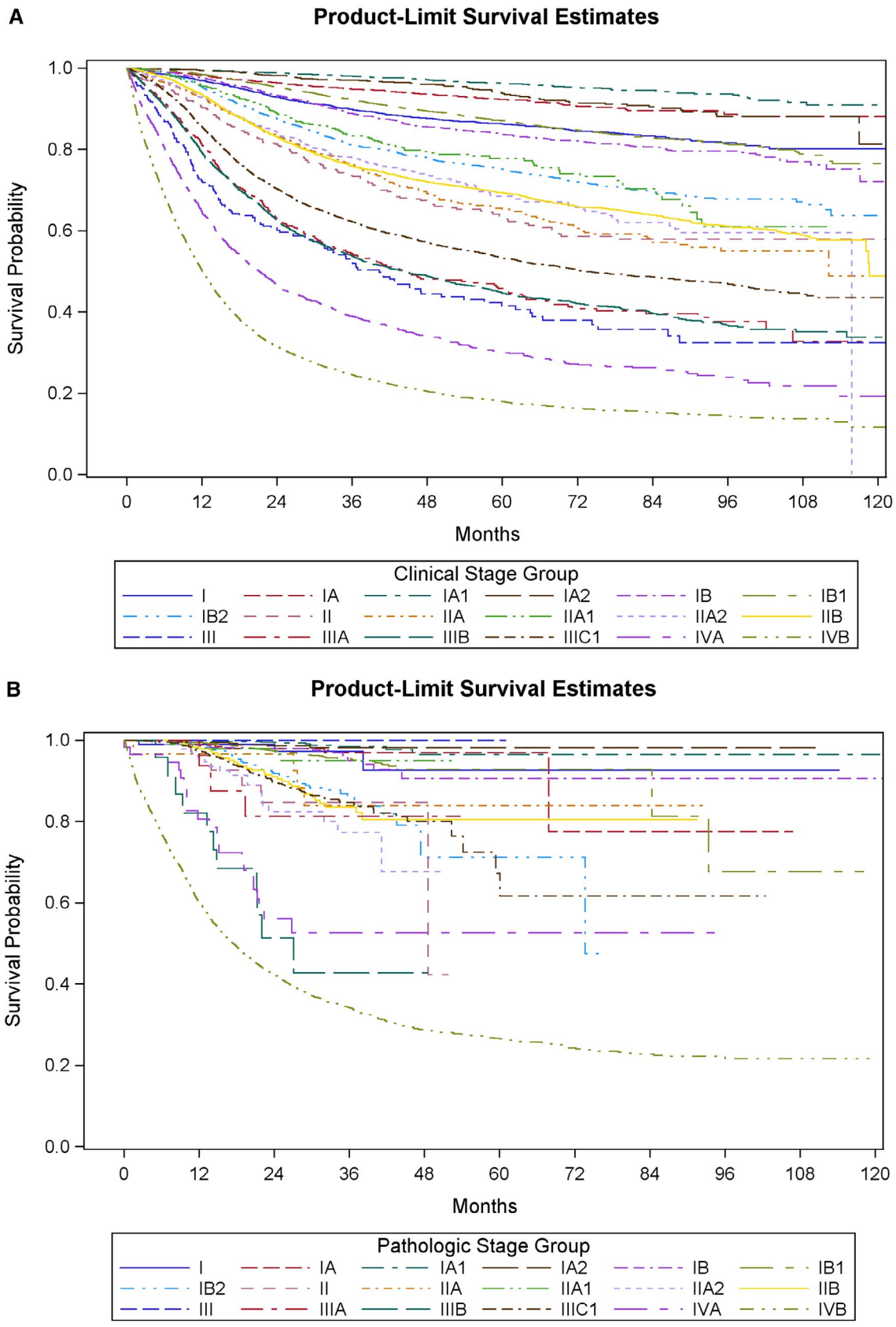

FIGURE 4. (A,B) Overall Survival Estimates by Stage Groupings.

M Category Changes

Similar to other categories, findings from cross-sectional imaging, fine-needle aspiration, core-needle biopsy, incisional biopsy, excisional biopsy, and surgical resections are all allowed to be used in designating the M category for the AJCC version 9 cervical cancer TNM staging. Previous versions of TNM staging allowed the incorporation of findings from distant metastases to influence M category designation only if such metastases were detectable by physical examination or plain x-ray. The new AJCC version 9 cervical cancer TNM staging M category update aligns cervical cancer workup and TNM staging very closely with treatment decision making and prognosis. A complete description of the M category is provided in Table 7. Survival estimates by clinical and pathologic M categories using NCDB data (2010-2017) are depicted in Figure 3A,B, with the corresponding number of patients at risk shown in Tables 8 and 9.

Stage Groups

All 3 categories, T, N, and M, are logically combined to generate the stage groups for the AJCC version 9 cervical cancer TNM staging. The stage groups are perfectly aligned with FIGO staging and compliant with the updated rules described in Chapter 1 of the *AJCC Cancer Staging Manual*, eighth edition (General Information on Cancer Staging and End Results Reporting).[18] Prognostic stage groups are shown in Table 10. Survival estimates by clinical and pathologic stage groups using NCDB data (2010-2017) are depicted in Figure 4A,B, with the corresponding number of patients at risk shown in Tables 11 and 12.

Conclusion

The AJCC version 9 TNM staging for cervical cancer heralds the AJCC version 9 system. This new cervical cancer TNM staging aligns with the recently published FIGO cervical cancer staging. The AJCC version 9 TNM staging for cervical cancer is an electronic product, was published in July of 2020, and went into use in the United States on January 1, 2021.■

Acknowledgments: We acknowledge the following: American Joint Committee on Cancer (AJCC) staff Donna Gress, Elaine Alexander, Chantel Ellis, and Martin Madera for their hard work toward launching version 9 of the TNM staging system; all members of the AJCC Executive Council and the AJCC Female Reproductive Panel, without whom this work would not have been possible; and the National Cancer Data Base management staff Bryan E. Palis and Amanda Browner.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68:394-424.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin.* 2020;70:7-30.
3. Bhatla N, Berek JS, Cuello Fredes M, et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet.* 2019;145:129-135.
4. Olawaiye AB, Hagemann I, Otis C, et al. AJCC Cancer Staging System for Cervix Uteri. Version 9. American College of Surgeons; 2020.
5. World Health Organization (WHO) Classification of Tumours Editorial Board, eds. Female Genital Tumours. WHO Classification of Tumours. 5th ed. Volume 4. International Agency for Research on Cancer; 2020.
6. Nicolas I, Marimon L, Barnadas E, et al. HPV-negative tumors of the uterine cervix. *Mod Pathol.* 2019;32:1189-1196.
7. Rodriguez-Carunchio L, Soveral I, Steenbergen RDM, et al. HPV-negative carcinoma of the uterine cervix: a distinct type of cervical cancer with poor prognosis. *BJOG.* 2015;122:119-127.
8. Higgins GD, Davy M, Roder D, Uzelin DM, Phillips GE, Burrell CJ. Increased age and mortality associated with cervical carcinomas negative for human papillomavirus RNA. *Lancet.* 1991;338:910-913.
9. McCluggage WG, Judge MJ, Alvarado-Cabrero I, et al. Data set for the reporting of carcinomas of the cervix: recommendations from the International Collaboration on Cancer Reporting (ICCR). *Int J Gynecol Pathol.* 2018;37:205-228.
10. Canaz E, Ozyurek ES, Erdem B, et al. Preoperatively assessable clinical and pathological risk factors for parametrial involvement in surgically treated FIGO stage IB-IIA cervical cancer. *Int J Gynecol Cancer.* 2017;27:1722-1728.
11. Frumovitz M, Sun CC, Schmeler KM, et al. Parametrial involvement in radical hysterectomy specimens for women with early-stage cervical cancer. *Obstet Gynecol.* 2009;114:93-99.
12. Kato T, Takashima A, Kasamatsu T, et al. Clinical tumor diameter and prognosis of patients with FIGO stage IB1 cervical cancer (JCOG0806-A). *Gynecol Oncol.* 2015;137:34-39.
13. Monk BJ, Wang J, Im S, et al. Rethinking the use of radiation and chemotherapy after radical hysterectomy: a clinical-pathologic analysis of a Gynecologic Oncology Group/Southwest Oncology Group/Radiation Therapy Oncology Group trial. *Gynecol Oncol.* 2005;96:721-728.
14. Dai YF, Xu M, Zhong LY, et al. Prognostic significance of solitary lymph node metastasis in patients with stages IA2 to IIA cervical carcinoma. *J Int Med Res.* 2018;46:4082-4091.
15. Lee YN, Wang KL, Lin MH, et al. Radical hysterectomy with pelvic lymph node dissection for treatment of cervical cancer: a clinical review of 954 cases. *Gynecol Oncol.* 1989;32:135-142.
16. Grigsby PW, Lu JD, Mutch DG, Kim RY, Eifel PJ. Twice-daily fractionation of external irradiation with brachytherapy and chemotherapy in carcinoma of the cervix with positive para-aortic lymph nodes: phase II study of the Radiation Therapy Oncology Group 92-10. *Int J Radiat Oncol Biol Phys.* 1998;41:817-822.
17. Olawaiye AB, Mutch DG. Lymphnode staging update in the American Joint Committee on Cancer 8th edition cancer staging manual. *Gynecol Oncol.* 2018;150:7-8.
18. American Joint Committee on Cancer (AJCC). General Information on Cancer Staging and End Results Reporting. In: Amin MB, Edge SB, Greene F, et al, eds. AJCC Cancer Staging Manual. 8th ed. Springer; 2017:3-52.