Carcinoma of the Cervix Uteri

JL BENEDET, F ODICINO, P MAISONNEUVE, U BELLER, WT CREASMAN, APM HEINTZ, HYS NGAN and S PECORELLI

STAGING

Anatomy

Primary site
The cervix is the lower third of the uterus. It is roughly cylindrical in shape, projects through the upper, anterior vaginal wall and communicates with the vagina through an orifice called the external os. Cancer of the cervix may originate on the vaginal surface or in the canal.

Nodal stations
The cervix is drained by preureteral, postureteral, and uterosacral routes into the following first station nodes: parametrial, internal (obturator – hypogastric), external iliac, presacral and common iliac. Para-aortic nodes are second station and are considered metastases.

Metastatic sites
The most common sites of distant spread include the aortic and mediastinal nodes, the lungs and skeleton.

Table 1
Carcinoma of the cervix uteri: FIGO nomenclature (Montreal, 1994)

Stage 0		Carcinoma *in situ*, cervical intraepithelial neoplasia Grade III.
Stage I		The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded).
	Ia	Invasive carcinoma which can be diagnosed only by microscopy. All macroscopically visible lesions – even with superficial invasion – are allotted to Stage Ib carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.0 mm and a horizontal extension of not >7.0 mm. Depth of invasion should not be >5.0 mm taken from the base of the epithelium of the original tissue – superficial or glandular. The involvement of vascular spaces – venous or lymphatic – should not change the stage allotment.
	Ia1	Measured stromal invasion of not >3.0 mm in depth and extension of not >7.0 mm.
	Ia2	Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm.
	Ib	Clinically visible lesions limited to the cervix uteri or preclinical cancers greater than Stage Ia.
	Ib1	Clinically visible lesions not >4.0 cm.
	Ib2	Clinically visible lesions >4.0 cm.
Stage II		Cervical carcinoma invades beyond uterus, but not to the pelvic wall or to the lower third of vagina.
	IIa	No obvious parametrial involvement.
	IIb	Obvious parametrial involvement.
Stage III		The carcinoma has extended to the pelvic wall. On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina. All cases with hydronephrosis or nonfunctioning kidney are included, unless they are known to be due to other cause.
	IIIa	Tumor involves lower third of the vagina, with no extension to the pelvic wall.
	IIIb	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney.
Stage IV		The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV.
	IVa	Spread of the growth to adjacent organs.
	IVb	Spread to distant organs.

Rules for classification

Clinical–diagnostic staging
Staging of cervical cancer is based on clinical evaluation; therefore, careful clinical examination should be performed in all cases, preferably by an experienced examiner and under anesthesia. The clinical staging must not be changed because of subsequent findings. When there is doubt as to which stage a particular cancer should be allocated, the earlier stage is mandatory. The following examinations are permitted: palpation, inspection, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography, and X-ray examination of the lungs and skeleton. Suspected bladder or rectal involvement should be confirmed by biopsy and histologic evidence. Conization or amputation of the cervix is regarded as a clinical examination. Invasive cancers so identified are to be included in
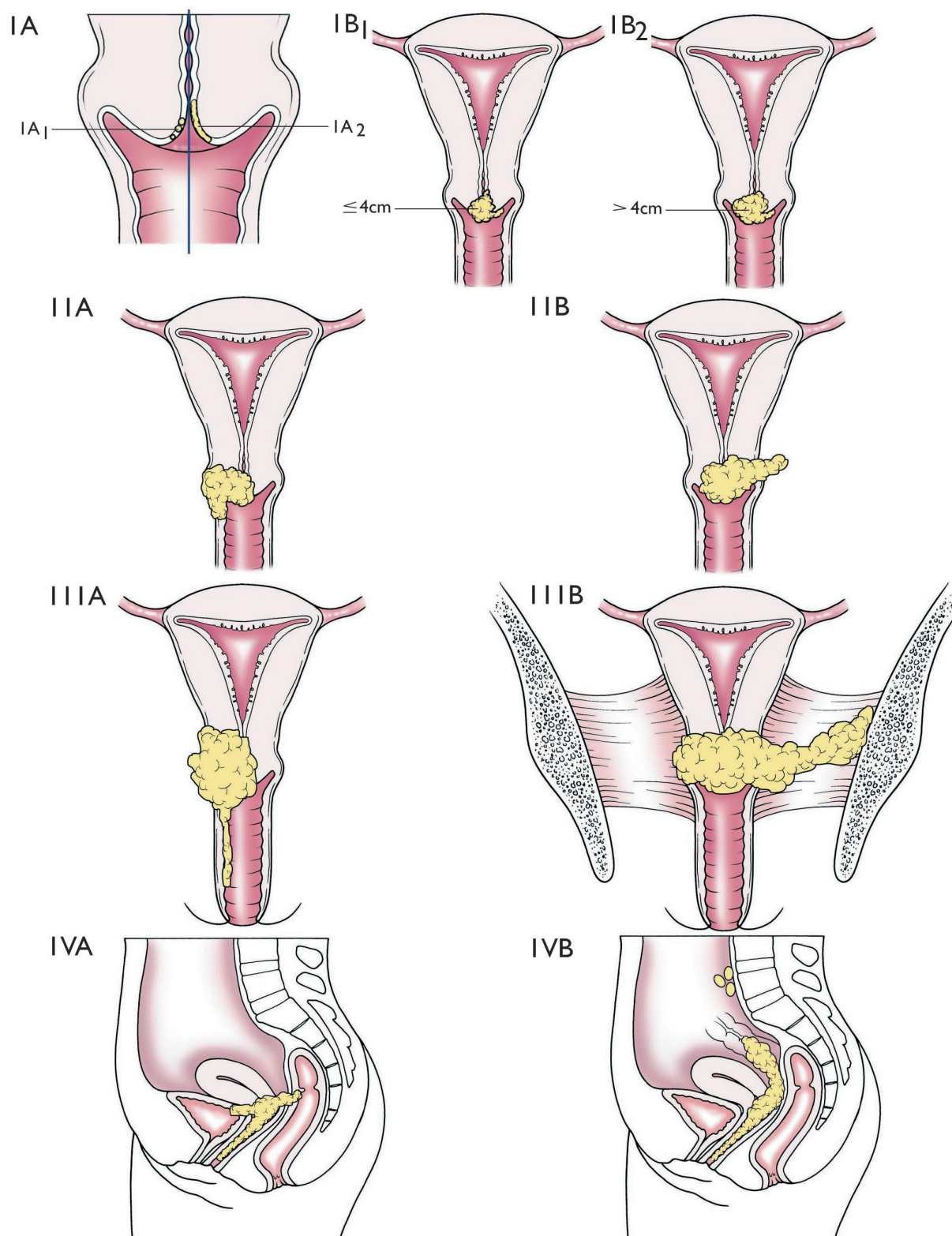
Fig. 1. Carcinoma of the cervix uteri: staging cervical cancer (primary tumor and metastases).

the reports. Findings of optional examinations e.g. lymphangiography, arteriography, venography, laparoscopy, ultrasound, computed tomography scan, and MRI are of value for planning therapy but, because these are not generally available and the interpretation of results is variable, the findings of such studies should not be the basis for changing the clinical staging. Fine needle aspiration (FNA) of scan-detected suspicious lymph nodes may be helpful in treatment planning.

Postsurgical treatment – pathologic staging
In cases treated by surgical procedures, the pathologist's findings in the removed tissues can be the basis for extremely accurate statements on the extent of disease. The findings should not be allowed to change the clinical staging but should be recorded in the manner described for the pathologic staging of disease. The TNM nomenclature is appropriate for this purpose. Infrequently it happens that hysterectomy is carried out in the presence of unsuspected extensive invasive cervical carcinoma. Such cases cannot be clinically staged or included in therapeutic statistics, but it is desirable that they be reported separately.

As in all gynecological cancers, staging is determined at the time of the primary diagnosis and cannot be altered, even at recurrence.

Only if the rules for clinical staging are strictly observed will it be possible to compare results among clinics and by differing modes of therapy.

Staging classification

Notes about the staging
Stage 0 comprises those cases with full-thickness involvement of the epithelium with atypical cells, but with no signs of invasion into the stroma.

The diagnosis of both Stage Ia1 and Ia2 should be based on microscopic examination of removed tissue, preferably a cone biopsy, which must include the entire lesion. The depth of invasion should not be >5 mm taken from the base of the epithelium, either surface or glandular, from which it originates. The second dimension, the horizontal spread, must not exceed 7 mm. Vascular space involvement, either venous or lymphatic, should not alter the staging, but should be specifically recorded because it may affect treatment decisions in the future. Larger lesions should be staged as Ib.

As a rule, it is impossible to clinically estimate if a cancer of the cervix has extended to the corpus. Extension to the corpus should therefore be disregarded.

A patient with a growth fixed to the pelvic wall by a short and indurated, but not nodular, parametrium should be allotted to Stage IIb. It is impossible, at clinical examination, to decide whether a smooth and indurated parametrium is truly cancerous or only inflammatory. Therefore, the case should be placed in Stage III only if the parametrium is nodular to the pelvic wall or if the growth itself extends to the pelvic wall.

The presence of hydronephrosis or non-functioning kidney resulting from stenosis of the ureter by cancer permits a case to be allotted to Stage III even if, according to the other findings, the case should be allotted to Stage I or Stage II.

The presence of bullous edema, as such, should not permit a case to be allotted to Stage IV. Ridges and furrows into the bladder wall should be interpreted as signs of submucous involvement of the bladder if they remain fixed to the growth at rectovaginal examination. Finding malignant cells in cytologic washings from the urinary bladder requires further histological confirmation in order to be considered for Stage IVa.

Histopathology

Cases should be classified as carcinomas of the cervix if the primary growth is in the cervix. All histologic types must be included. Grading by any of several methods is encouraged, but is not a basis for modifying the stage groupings. When surgery is the primary treatment, the histologic findings permit the case to have pathologic staging, as described above. In this situation, the TNM nomenclature may be used. All tumors are to be microscopically verified.

Histopathologic types
- Cervical intraepithelial neoplasia, Grade III
- Squamous cell carcinoma *in situ*
- Squamous cell carcinoma
  – Keratinizing
  – Nonkeratinizing
  – Verrucous
- Adenocarcinoma *in situ*
- Adenocarcinoma *in situ*, endocervical type
- Endometrioid adenocarcinoma
- Clear cell adenocarcinoma
- Adenosquamous carcinoma
- Adenoid cystic carcinoma
- Small cell carcinoma
- Undifferentiated carcinoma

Histopathologic grade (G)
- GX: Grade cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly or undifferentiated

Table 2
Carcinoma of the cervix uteri: Stage grouping for cervix uteri

FIGO Stage	UICC		
	T	N	M
0	Tis	N0	M0
Ia1	T1a1	N0	M0
Ia2	T1a2	N0	M0
Ib1	T1b1	N0	M0
Ib2	T1b2	N0	M0
IIa	T2a	N0	M0
IIb	T2b	N0	M0
IIIa	T3a	N0	M0
IIIb	T1	N1	M0
	T2	N1	M0
	T3a	N1	M0
	T3b	any N	M0
IVa	T4	any N	M0
IVb	any T	any N	M1

DEFINITIONS OF TREATMENTS

Treatment definitions are given in Table 3.

Table 3
Carcinoma of the cervix uteri: Definitions of treatments

Treatment	Definition
None	No treatment.
Surgery alone	Surgery as first therapy and no other therapy(ies) within 90 days from the date of surgery. Subsequently, patients can be given any further treatment.
Radiotherapy alone	External radiotherapy and/or intracavitary irradiation as first therapy(ies) and no other therapy(ies) within 90 days from the end of teletherapy/brachytherapy. Subsequently, patients can be given any further treatment.
Radio-surgery	External radiotherapy/intracavitary irradiation as first therapy and then surgery within 90 days from the end of teletherapy/brachytherapy. Subsequently, patients can be given any further treatment. (Chemotherapy can be associated within 120 days from the date of surgery.)
Neoadjuvant chemotherapy + surgery	Chemotherapy as first therapy and then surgery within 42 days from the end of chemotherapy. Subsequently, patients can be given any further treatment.
Surgery + adjuvant radiotherapy	Surgery as first therapy and then radiotherapy within 90 days from the date of surgery. Subsequently, patients can be given any further treatment. (Chemotherapy can be associated within 120 days from the date of surgery.)
Surgery + adjuvant chemotherapy	Surgery as first therapy and then chemotherapy within 90 days from the date of surgery or of the end of radiotherapy.
Chemo-radiotherapy	Radiotherapy with chemotherapy (either neoadjuvant, concomitant or sequential) administered together or at least within 90 days from the end of either therapy.
Chemotherapy alone	Chemotherapy as first therapy and no other therapy(ies) within 90 days from the end of chemotherapy. Subsequently, patients can be given any further treatment.

DATA ANALYSIS

Summary and comments

Volume 25 of the Annual Report contains information on an additional 13 982 patients treated for cervical cancer since the previous Volume which was published in 2000. This total represents results submitted by 80 different international centers and represents an increase in both the number of cases treated, as well as the number of reporting institutions contributing data to this report. The increase in the total number of cases reported in this Volume reverses a trend that had been noted in Volumes 23 and 24 where the actual numbers of cervical cancers had shown a decline. It should be stressed that rather than indicating any overall worldwide trends these numbers are simply a reflection of the total number of cases reported from individual contributing institutions and do not reflect national incidence rates for this disease.

Table 4 lists the number of cases by stage for each of the reporting institutions. As expected the number of cases per institution reflects not only the frequency of cervical cancers in certain parts of the globe but also the fact that many of the reporting institutions are highly specialized centers which serve as regional referral centers for assessment and management of these

Table 4
Carcinoma of the cervix uteri: patients treated in 1996–98. Distribution of patients by center and stage

		All	Not available	Stage I	Stage II	Stage III	Stage IV
All centers		13982	192	5491	4403	3315	581
Nigeria	Ibadan (I Adewole)	120	4	16	43	45	12
South Africa	Pretoria (G Lindeque)	199	1	57	37	91	13
Argentina	Buenos Aires (R Testa)	24	–	12	11	–	1
	Neuquén (GH Focaccia)	72	–	12	33	21	6
	Santa Fe (A Ellena)	33	–	11	10	9	3
Brazil	Belo Horizonte (A Moraes de Souza)	448	–	56	271	120	1
	Porto Alegre (G Py Gomez da Silveira)	52	–	23	10	18	1
Canada	Montreal (GW Stanimir)	5	–	–	–	4	1
Chile	Santiago (E Suarez)	146	–	97	36	12	1
	Temuco (I Capurro)	146	11	71	28	25	11
Peru	Arequipa (L Medina Fernandez)	77	–	11	22	38	6
USA	Baltimore MA (F Montz, RE Bristow)	58	18	22	5	9	4
	Columbus OH (J Fowler)	154	–	87	30	25	12
	Jacksonville FL (BU Sevin)	16	–	5	8	1	2
	Nashville TN (HW Jones)	99	–	61	20	12	6
	New York NY (R Barakat)	151	53	62	16	14	6
	Orange CA (PJ DiSaia)	91	1	58	18	9	5
Uruguay	Montevideo (G Arribeltz)	62	–	38	10	12	2
China	Guangzhou (J Liu)	365	19	115	153	70	8
	Hong Kong (HYS Ngan)	228	4	119	58	40	7
	Hong Kong (VSY Yu)	85	–	33	39	13	–
	Wuhan (S Yu)	84	–	2	21	61	–
Indonesia	Medan (M Fauzie Sahil)	137	–	20	48	57	12
Japan	Kumamoto (H Okamura)	105	–	59	19	17	10
	Nagasaki (T Ishimaru)	88	–	50	26	6	6
	Osaka (A Suzuki)	187	–	94	59	20	14
	Tokyo (K Kinoshita)	43	–	19	22	1	1
	Sagamihara (H Kuramoto)	154	–	111	21	19	3
Korea	Seoul (HP Lee)	348	5	237	97	8	1
	Seoul (JE Mok)	250	–	169	58	14	9
Philippines	Manila (IB Benitez)	48	–	17	21	8	2
	Manila (AM Manalo)	995	48	142	351	455	43
Taiwan	Taoyuan (TC Chang)	969	9	562	270	92	36
Thailand	Bangkok (V Linasmita)	412	–	63	193	146	10
	Songkhla (V Wootipoom)	693	2	133	293	219	46
Austria	Graz (R Winter)	158	–	89	42	20	7
	Innsbruck (C Marth)	140	–	67	22	37	10
Croatia	Zagreb (S Jukić)	215	–	85	69	50	11
Czech Republic	Brno (A Dörr)	328	–	89	51	172	16
	Prague (E Kmonícková)	178	–	59	60	43	16

Table 4, *continued*

		All	Not available	Stage I	Stage II	Stage III	Stage IV
Finland	Jyväskylä (H Sundström)	19	–	7	5	5	2
	Turku (T Salmi)	38	–	18	10	5	5
France	Bordeaux (ML Campo)	103	–	35	49	14	5
	Grenoble (P Bernard)	18	–	8	2	2	6
	Lille (E Leblanc)	129	–	34	42	42	11
Germany	Hannover (H Kühnle)	83	–	47	20	5	11
	Jena (A Schneider)	136	–	75	44	10	7
	Kiel (D Weisner)	126	–	72	20	27	7
	Würzburg (H Caffier)	109	23	36	31	11	8
Greece	Athens (S Michalas)	51	7	18	17	8	1
Italy	Brescia (SM Magrini)	88	–	29	48	8	3
	Brescia (S Pecorelli)	59	–	46	8	3	2
	Genova (N Ragni)	18	–	8	8	2	–
	Trento (E Arisi)	7	–	4	2	–	1
Netherlands	Amsterdam (MPM Burger)	221	–	128	58	26	9
Poland	Kraków (K Urbanski)	450	1	213	170	63	3
	Łódź (J Sobotkowski)	352	1	82	116	124	29
	Wrocław (J Kornafel, J Błaszczyk)	527	–	175	175	177	–
Portugal	Coimbra (C Freire de Oliveira)	65	–	19	17	23	6
	Coimbra (D Pereira da Silva)	39	–	16	13	9	1
	Coimbra (O Campos)	177	17	60	40	53	7
	Lisboa (MA Roldão)	499	–	152	266	70	11
	Porto (MT Osorio)	426	–	145	181	80	20
Romania	Cluj-Napoca (L Lazar, L Neamtiu)	415	–	102	109	200	4
Slovakia	Bratislava (J Kállay)	225	–	158	49	14	4
Slovenia	Maribor (I Takač)	60	1	23	11	21	4
Spain	Barcelona (S Dexeus)	27	–	17	6	2	2
	Barcelona (J Pahisa Fabregas)	68	–	36	19	7	6
	Barcelona (A Gil Moreno)	48	–	36	11	–	1
	Cruces-Baracaldo (FJ Rodríguez Escudero)	57	–	39	11	7	–
	Las Palmas de Gran Canaria (O Falcón Vizcaino)	90	–	47	30	10	3
	Madrid (F Calero Cuerda)	70	–	43	9	15	3
	Madrid (P de La Fuente)	48		29	9	8	2
Sweden	Gothenburg (G Horvath)	178	–	85	46	37	10
	Örebro (B Sorbe)	111	–	71	17	14	9
Switzerland	Basel (W Holzgreve)	8	–	–	2	5	1
United Kingdom	Northwood (PJ Hoskin)	82	4	25	30	19	4
Yugoslavia	Beograd (V Kesic)	146	–	130	16	–	–
	Kladovo (B Ristić)	304	–	87	61	149	7
Australia	Carlton (M Quinn)	142	3	103	24	7	5

Table 5
Carcinoma of the cervix uteri: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage I), $n = 5491$

Country	Number of patients	First line of treatment (%)									
		None	Surgery alone	RT alone	Radio-surgery	Neoadj CT + surg	Surg + adj RT	Surg + adj CT	CT + RT	CT alone	Other non-standard
All	5491	1	46	13	7	2	25	3	1	0	3
Nigeria	16	–	–	81	19	–	–	–	–	–	–
South Africa	57	–	72	7	2	–	19	–	–	–	–
Argentina	35	–	63	3	–	6	29	–	–	–	–
Brazil	79	–	27	47	4	1	20	–	–	–	1
Chile	168	2	29	21	38	–	10	–	–	–	1
Peru	11	–	36	27	–	–	36	–	–	–	–
USA	295	1	66	5	1	1	20	5	1	–	–
Uruguay	38	3	71	13	3	–	11	–	–	–	–
China	269	2	42	16	7	0	16	3	2	–	12
Indonesia	20	15	60	10	–	–	15	–	–	–	–
Japan	333	–	76	5	0	0	13	5	–	–	1
Korea	406	0	71	1	1	14	9	2	1	–	1
Philippines	159	19	10	35	4	1	13	1	5	1	11
Taiwan	562	1	62	12	1	6	15	3	1	0	–
Thailand	196	4	50	34	6	1	5	–	–	–	–
Austria	156	1	71	6	–	1	14	8	–	–	–
Croatia	85	–	8	21	31	–	16	–	6	–	18
Czech Republic	148	–	43	4	–	1	47	2	1	–	3
Finland	25	–	24	–	8	–	68	–	–	–	–
France	77	–	25	18	31	1	25	–	–	–	–
Germany	230	0	66	6	–	–	23	3	–	–	2
Greece	18	–	39	–	–	6	56	–	–	–	–
Italy	87	–	37	20	–	10	21	9	–	–	3
Netherlands	128	–	69	9	–	–	21	–	–	–	1
Poland	470	–	10	21	9	–	60	0	–	–	0
Portugal	392	1	25	22	32	–	18	1	–	–	1
Romania	102	–	23	1	35	1	28	–	–	–	12
Slovakia	158	–	34	3	–	1	56	2	–	–	5
Slovenia	23	–	61	22	9	–	9	–	–	–	–
Spain	247	–	62	9	1	2	25	–	–	–	0
Sweden	156	1	49	3	2	–	17	27	1	–	1
UK	25	–	–	16	–	16	60	–	–	–	8
Yugoslavia	217	–	15	1	–	–	83	–	–	–	–
Australia	103	2	39	3	–	–	16	–	1	–	40

cancers. Table 4 also shows that, while 70% of the reported cases are Stage I or II, a disappointing 30% are Stage III or IV at the time of diagnosis. Unfortunately these percentages have changed little from those of the previous two Annual Reports.

Table 5 represents total number of patients treated in 1996 and 1998 by the various treatment methods previously defined. As expected a majority (46%) of patients with Stage I disease were treated with surgery alone. An additional 25% had surgery with adjuvant radiotherapy. These two treatment approaches were used in 71% of patients. Radiotherapy alone was used in 13% of patients and was the third most commonly used treatment method in patients with Stage I disease. The actual numbers of women treated by radiotherapy in each institution varied considerably with some institutions treating a large number of patients with this modality.

Table 6 presents the treatment results by country and treatment method for individuals presenting with Stage II

disease. Radiotherapy alone was used in 65% of patients with an additional 10% treated with surgery and adjuvant radiotherapy. A trend to increasing use of radiotherapy with increasing stage of disease was noted, with 74% of patients with Stage III disease treated in this manner (Table 7). Some countries treated over 90% of patients with radiotherapy for Stage III disease. As expected there was an increasing trend to the use of chemotherapy either as stand alone treatment or in conjunction with other modalities with advancing stage of disease. This is a continuation of the pattern that was first noted in Volume 24.

Table 6
Carcinoma of the cervix uteri: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage II), $n = 4403$

Country	Number of patients	First line of treatment (%)									
		None	Surgery alone	RT alone	Radio-surgery	Neoadj CT + surg	Surg + adj RT	Surg + adj CT	CT + RT	CT alone	Other non-standard
All	4403	3	3	65	6	3	10	2	5	0	4
Nigeria	43	–	–	81	19	–	–	–	–	–	–
South Africa	37	–	5	81	–	3	3	–	8	–	–
Argentina	54	2	2	19	–	11	7	–	54	4	2
Brazil	281	–	1	93	1	–	5	–	0	–	0
Chile	64	3	–	69	27	–	2	–	–	–	–
Peru	22	–	–	100	–	–	–	–	–	–	–
USA	97	3	11	46	3	2	16	5	11	–	1
Uruguay	10	10	10	20	10	–	30	–	20	–	–
China	271	2	2	44	16	1	8	0	6	0	20
Indonesia	48	2	2	96	–	–	–	–	–	–	–
Japan	147	–	18	16	1	6	38	15	3	–	3
Korea	155	1	9	16	–	32	15	5	13	2	6
Philippines	372	25	1	58	1	–	2	–	4	–	9
Taiwan	270	1	10	57	1	5	9	1	13	1	–
Thailand	486	4	–	87	7	–	–	–	1	–	–
Austria	64	2	16	34	–	3	14	28	2	–	2
Croatia	69	–	–	33	38	3	9	–	14	–	3
Czech Republic	111	–	1	73	1	1	14	–	8	–	3
Finland	15	–	13	40	20	–	20	–	7	–	–
France	93	–	–	61	27	–	9	–	1	–	2
Germany	115	1	16	21	–	1	49	3	1	–	9
Greece	17	–	–	65	–	–	24	–	12	–	–
Italy	66	–	–	65	2	9	18	2	2	–	3
Netherlands	58	–	12	76	–	–	12	–	–	–	–
Poland	461	0	–	95	2	–	3	–	0	–	–
Portugal	517	0	0	92	5	0	1	–	1	–	–
Romania	109	–	–	28	49	–	1	–	6	–	17
Slovakia	49	–	–	18	2	14	51	–	8	–	6
Slovenia	11	–	45	55	–	–	–	–	–	–	–
Spain	95	2	4	48	–	12	21	–	4	–	8
Sweden	63	–	3	43	2	–	10	32	2	–	10
Switzerland	2	–	–	–	–	50	50	–	–	–	–
UK	30	–	–	47	–	10	23	–	20	–	–
Yugoslavia	77	–	–	34	–	–	66	–	–	–	–
Australia	24	4	8	8	–	–	25	–	–	–	54

The mean age by stage and histologic type for the patients treated in Volume 25 is presented in Table 10. The mean ages of the various stages showed a gradual increase with advancing stage for all histologic sub-types with the actual values remarkably similar for each sub-stage category regardless of histologic type. This data would suggest that for the most part cervical cancer continues to be a disease of peri-menopausal and post-menopausal women.

Table 11 shows the actual number of patients treated

Table 7
Carcinoma of the cervix uteri: patients treated in 1996-98. Distribution of patients (%) by country and treatment (Stage III), $n = 3315$

Country	Number of patients	First line of treatment (%)									
		None	Surgery alone	RT alone	Radio-surgery	Neoadj CT + surg	Surg + adj RT	Surg + adj CT	CT + RT	CT alone	Other non-standard
All	3315	9	0	74	1	1	2	0	9	0	3
Nigeria	45	–	–	93	4	–	2	–	–	–	–
South Africa	91	5	–	91	–	–	1	–	1	1	–
Argentina	30	–	–	53	–	3	–	–	40	3	–
Brazil	138	–	–	96	–	–	3	–	1	–	–
Canada	4	–	–	75	–	–	–	–	25	–	–
Chile	37	5	–	95	–	–	–	–	–	–	–
Peru	38	–	–	100	–	–	–	–	–	–	–
USA	70	7	9	31	1	3	19	3	23	1	1
Uruguay	12	–	–	58	–	–	8	–	33	–	–
China	184	3	–	72	–	–	1	–	19	–	5
Indonesia	57	2	–	98	–	–	–	–	–	–	–
Japan	63	–	2	51	–	11	–	3	19	3	11
Korea	22	5	–	18	–	5	5	5	59	–	5
Philippines	463	50	1	37	–	0	–	0	3	–	8
Taiwan	92	3	–	63	2	–	–	–	28	–	–
Thailand	365	5	–	89	1	–	0	–	4	–	–
Austria	57	5	–	72	–	5	–	–	9	7	2
Croatia	50	–	–	52	4	–	–	–	44	–	–
Czech Republic	215	–	–	77	–	–	3	–	19	–	1
Finland	10	20	10	50	–	10	–	–	10	–	–
France	58	–	–	69	12	–	7	–	12	–	–
Germany	53	2	4	66	–	–	13	–	6	–	9
Greece	8	–	–	100	–	–	–	–	–	–	–
Italy	13	–	–	54	–	–	–	–	38	8	–
Netherlands	26	–	–	96	4	–	–	–	–	–	–
Poland	364	1	–	98	–	–	–	–	0	–	0
Portugal	235	5	–	90	0	–	1	0	3	–	–
Romania	200	–	–	56	10	–	1	–	24	–	10
Slovakia	14	–	–	86	7	7	–	–	–	–	–
Slovenia	21	10	–	86	–	–	5	–	–	–	–
Spain	49	12	–	61	–	2	–	–	14	–	10
Sweden	51	4	–	69	–	–	–	–	4	–	24
Switzerland	5	–	–	60	–	–	20	–	20	–	–
UK	19	–	–	58	–	–	16	–	11	–	16
Yugoslavia	149	–	–	97	1	–	2	–	–	–	–
Australia	7	14	–	–	–	–	29	–	–	–	57

in 1996–1998 by stage and histologic type. Overall, 79.2% of all patients treated had epidermoid lesions with an additional 10.9% treated for adenocarcinoma. Mixed adenosquamous cancers were relatively uncommon and were responsible for 4.4% of the total number of patients treated. This distribution of cases was similar to that reported in the previous Volumes. There was a marked decrease in the number of cases where the histologic type was not stated or was missing indicating an overall improvement in the quality of the reports submitted.

Table 12 represents the number and percentage of patients treated in 1996–1998 with the actual correlation

Table 8
Carcinoma of the cervix uteri: patients treated in 1996–98. Distribution of patients (%) by country and treatment (Stage IV), $n = 581$

Country	Number of patients	First line of treatment (%)									
		None	Surgery alone	RT alone	Radio-surgery	Neoadj CT + surg	Surg + adj RT	Surg + adj CT	CT + RT	CT alone	Other non-standard
All	581	17	2	48	2	2	3	1	15	6	5
Nigeria	12	–	–	75	25	–	–	–	–	–	–
South Africa	13	15	–	85	–	–	–	–	–	–	–
Argentina	10	40	–	20	–	10	–	–	30	–	–
Brazil	2	–	–	100	–	–	–	–	–	–	–
Canada	1	100	–	–	–	–	–	–	–	–	–
Chile	12	67	–	25	–	–	–	–	–	–	–
Peru	6	–	–	100	–	–	–	–	–	–	–
USA	35	6	11	26	3	–	14	3	14	20	3
Uruguay	2	–	–	100	–	–	–	–	–	–	–
China	15	7	–	53	–	–	7	–	20	–	13
Indonesia	12	33	–	67	–	–	–	–	–	–	–
Japan	34	3	3	35	–	3	–	3	38	9	6
Korea	10	10	–	30	–	20	–	–	30	10	–
Philippines	45	67	–	27	–	–	–	–	–	–	7
Taiwan	36	14	3	33	–	–	–	–	44	6	–
Thailand	56	20	–	71	–	–	2	–	7	–	–
Austria	17	6	–	41	–	12	–	–	18	24	–
Croatia	11	9	–	64	–	–	9	–	9	9	–
Czech Republic	32	–	–	66	–	–	6	–	28	–	–
Finland	7	29	–	29	–	–	14	–	14	14	–
France	22	27	–	32	14	–	–	–	18	9	–
Germany	33	15	12	24	6	3	9	–	9	6	12
Greece	1	–	–	–	–	–	–	–	–	–	–
Italy	6	–	17	17	–	33	–	–	17	–	17
Netherlands	9	–	–	100	–	–	–	–	–	–	–
Poland	32	19	–	63	–	–	–	–	3	16	–
Portugal	45	9	–	71	–	–	–	–	18	2	–
Romania	4	–	–	25	–	–	–	–	75	–	–
Slovakia	4	–	–	25	–	–	25	–	25	25	–
Slovenia	4	–	–	75	–	–	–	25	–	–	–
Spain	17	12	–	24	–	6	–	6	12	18	24
Sweden	19	11	–	42	–	–	–	–	21	–	26
Switzerland	1	–	–	–	–	–	–	100	–	–	–
UK	4	–	–	50	–	–	–	–	25	–	25
Yugoslavia	7	–	–	86	–	–	–	–	–	–	14
Australia	5	–	–	20	–	–	–	–	–	–	80

between the FIGO stage (assessed clinically) and pT stage (TNM system) in patients treated with upfront surgery or surgery alone with or without adjuvant radiotherapy/ chemotherapy. These stage correlations, as one can see, were best for the earliest stages of disease and also for those with Stage IIIb or higher. Clearly, the assessment of parametrial infiltration is extremely difficult clinically and most likely accounts for the discrepancies between clinical and pathologic staging for individuals with clinical Stage Ib2, IIa as well as Stage IIIa disease. In particular, it is clear that a significant number of patients with Ib2 and IIa disease are found to have higher stage disease on surgical exploration. Conversely, 18% of patients with IIa disease had lower stage disease when primary surgery or combined surgery with radiotherapy was used as a treatment modality indicating the potential for more accurate staging when surgery is used in the management of these individuals.

Cervical cancer continues to be the only major gynecological malignancy that is not surgically staged at the present time. Recently, the move to surgically stage endometrial cancer was not without controversy and its acceptance was not readily endorsed by all centers, nonetheless, today virtually all major cancer centers surgically stage endometrial cancer and its value is well accepted by all clinicians. The FIGO Committee on Gynecologic Oncology constantly evaluates all current evidence-based medicine on surgical staging of carcinoma of the cervix uteri. Up till now, the Committee has decided not to modify the present clinical staging which is employed on a world-wide basis and, in particular, in countries with limited resources where cervical cancer is the major neoplasm affecting women between 30 and 50 years of age.

Table 9
Carcinoma of the cervix uteri: patients treated in 1996–98. Review of the 5-year survival rates reported in volumes 18–25

Vol.	Year	Patients	Survival (%)
18	1973–75	34178	55.7
19	1976–78	32428	55.0
20	1979–81	31543	53.5
21	1982–86	32052	59.8
22	1987–89	22428	65.0
23	1990–92	12153	65.4
24	1993–95	11709	72.2
25	**1996–98**	**10525**	**69.9**
Total		**187016**	

Table 10
Carcinoma of the cervix uteri: patients treated in 1996–98. Mean age by stage and histologic type

Histotype	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIa	IIIb	IVa	IVb
Epidermoid	44.5	45.9	48.5	46.6	55.6	52.8	55.8	54.3	57.7	54.4
Adenocarcinoma	43.3	48.3	46.8	48.3	53.6	53.2	55.1	55.5	58.9	59.0
Adenosquamous	42.4	38.2	45.3	45.9	51.6	53.1	54.1	54.6	59.9	56.5
Clear cell	–	32.0	45.6	53.3	48.8	61.9	56.0	56.4	54.0	53.5
Other	44.3	49.1	50.6	47.4	59.3	52.7	61.5	55.1	60.9	55.4

Table 11
Carcinoma of the cervix uteri: patients treated in 1996–98. Number of patients by stage and histologic type

Histotype	Missing	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIa	IIIb	IVa	IVb	Total	%
Missing/not stated	7	19	7	26	12	16	39	4	72	9	8	219	1.6
Epidermoid	67	818	246	2274	839	943	2685	261	2514	256	172	11075	79.2
Adenocarcinoma	32	55	36	492	176	103	314	30	222	27	40	1527	10.9
Adenosquamous	6	31	11	175	68	63	112	17	98	16	12	609	4.4
Clear cell	1	0	1	8	8	9	12	5	14	3	2	63	0.5
Other	79	29	8	103	49	36	71	13	65	21	15	489	3.5
Total	192	952	309	3078	1152	1170	3233	330	2985	332	249	13982	100.0

The overall survival for all treated patients after 5 years, by age groups and FIGO stages, is presented in Table 13. As expected, survival was predominately a function of stage with patient age being less important. Table 14 presents the number of patients treated in 1996–98 who relapsed by stage and site. Unfortunately, the information on the site of relapse was missing for the majority of patients and the data are too scarce to allow an overall picture on the site of relapse by stage.

Table 15 presents the response to treatment by stage for those patients treated between 1996 and 1998. Unfortunately, stage at diagnosis was reported as missing in a significant number of patients which in turn makes interpretation of some of this data difficult. However, as expected, only 12 to 45% of advanced stage patients (IIIa–IVb) completely responded to primary treatment, while in early stages the complete response rate to primary treatment ranged from 70 to 90%.

The survival curves by age at diagnosis for the various stages are presented in Figures 4–7.

Age, *per se*, represents a valuable prognostic factor in the early stages and, in multivariate analysis, it is an independent prognostic factor only for Stage I patients. Probably, this observation reflects a different opportunity to submit elderly patients to complete and effective therapies, rather than a different biological behavior of the disease in patients in this age group.

Although clinical staging for cervical cancer is not precise in defining the true pathological extent of the tumor (see Table 12), it can optimally define the patients' prognosis, as presented in Figure 9.

In the following figures, survival data on the type of primary treatment are presented.

For the 6873 patients who had a partial or complete response relapse-free survival was evaluated. Endpoint was either relapse or death, while patients still alive without disease at the end of the follow-up were right censored.

Table 12

Carcinoma of the cervix uteri: patients treated in 1996-98. Correlation % (number of patients) between FIGO stage (clinically assessed) and pT (TNM) in patients treated with upfront surgery (surgery alone ± adj RT/CT)

pT (TNM)	FIGO									
	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb
Ia1	**94%**	7%	3%	2%	3%	1%	1%	1%	2%	0%
	(544)	(13)	(55)	(13)	(10)	(9)	(1)	(3)	(1)	(0)
Ia2	2%	**82%**	2%	3%	1%	1%	0%	1%	0%	0%
	(14)	**(155)**	(39)	(15)	(4)	(4)	(0)	(2)	(0)	(0)
Ib1	3%	7%	**83%**	9%	10%	6%	1%	2%	4%	11%
	(15)	(14)	**(1618)**	(46)	(36)	(36)	(1)	(6)	(2)	(3)
Ib2	0%	2%	2%	**69%**	4%	1%	1%	1%	0%	0%
	(1)	(4)	(43)	**(365)**	(15)	(7)	(1)	(2)	(0)	(0)
IIa	0%	0%	2%	2%	**66%**	3%	1%	1%	0%	0%
	(2)	(0)	(40)	(10)	**(240)**	(18)	(1)	(4)	(0)	(0)
IIb	0%	1%	3%	6%	6%	**81%**	4%	3%	4%	4%
	(0)	(2)	(59)	(29)	(21)	**(509)**	(3)	(9)	(2)	(1)
IIIa	0%	1%	0%	0%	1%	0%	**78%**	0%	0%	4%
	(1)	(1)	(1)	(2)	(4)	(3)	**(54)**	(1)	(0)	(1)
IIIb	0%	1%	5%	8%	8%	6%	12%	**90%**	0%	4%
	(0)	(1)	(96)	(41)	(30)	(37)	(8)	**(276)**	(0)	(1)
IVa	0%	0%	0%	0%	1%	1%	0%	2%	**90%**	4%
	(0)	(0)	(2)	(2)	(3)	(4)	(0)	(5)	**(45)**	(1)
IVb	0%	0%	0%	1%	0%	1%	0%	0%	0%	**74%**
	(0)	(0)	(3)	(3)	(1)	(4)	(0)	(0)	(0)	**(20)**

Table 13
Carcinoma of the cervix uteri: patients treated in 1996–98. Overall survival (%) after 5 years by age groups and FIGO stage

Age at diagnosis	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb
15–29	100.0	86.7	87.5	76.0	78.2	52.7	–	35.1	33.3	–
30–39	100.0	100.0	87.5	80.0	67.3	62.6	–	46.6	12.8	13.4
40–49	98.8	97.5	90.7	78.3	69.1	67.0	45.0	43.0	36.5	21.5
50–59	97.3	100.0	89.1	85.9	70.3	73.1	43.2	46.4	18.6	17.4
60–69	96.6	82.6	88.6	77.1	73.2	64.9	43.7	45.0	22.4	16.4
70–79	93.2	87.5	76.2	81.2	68.3	54.9	36.5	42.2	10.3	–
80+	100.0	–	51.9	15.1	43.9	37.8	–	25.3	–	9.1
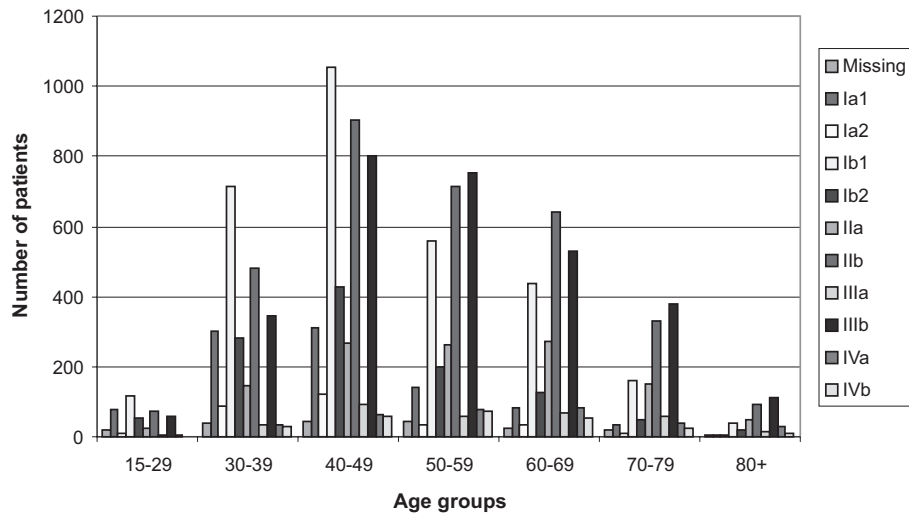
Age group	Missing	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb	Total
15–29	18	79	12	118	55	22	73	6	58	4	1	446
30–39	37	299	87	713	283	145	481	33	347	32	28	2485
40–49	44	310	123	1053	426	266	906	92	804	63	59	4146
50–59	42	139	36	557	197	262	714	60	752	80	72	2911
60–69	24	82	36	437	125	274	639	68	531	82	55	2353
70–79	20	36	12	162	47	150	330	57	381	41	22	1258
80+	7	7	3	38	19	51	90	14	112	30	12	383

Fig. 2. Carcinoma of the cervix uteri: patients treated in 1996–98. Distribution of patients by stage and age groups.

Table 14
Carcinoma of the cervix uteri: patients treated in 1996–98. Relapses by stage

Site of relapse	All	Missing	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb
Local (regional)	649	6	8	7	91	39	73	209	29	163	21	3
Metastatic	514	2	4	2	74	38	59	173	12	136	7	7
Local and metastatic	186	–	3	–	21	11	16	62	5	57	5	6
Missing site	7375	58	497	183	1883	580	647	1866	171	1356	90	44
Total	8724	66	512	192	2069	668	795	2310	217	1712	123	60
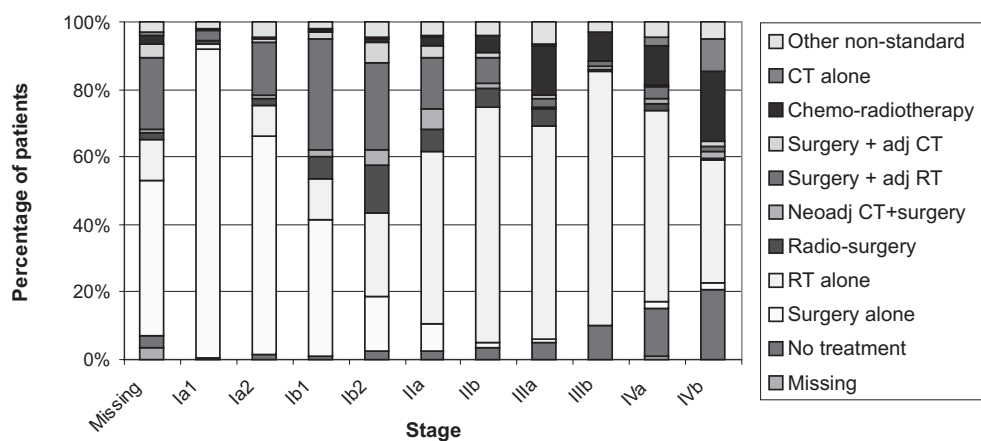
Treatment	Missing	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb	Total
Missing	7	1	0	2	0	0	2	0	7	3	0	22
No treatment	7	3	5	28	29	27	111	16	288	48	51	613
Surgery alone	88	870	200	1249	189	97	50	4	11	6	5	2769
RT alone	23	17	28	365	282	594	2250	209	2239	188	91	6286
Radio-surgery	4	7	6	209	162	80	183	16	25	7	2	701
Neoadj CT + surgery	2	2	3	63	53	72	48	1	17	5	5	271
Surgery + adj RT	41	28	49	1003	300	176	249	9	46	12	3	1916
Surgery + adj CT	7	2	2	73	66	40	41	4	3	1	4	243
Chemo-radiotherapy	5	1	2	16	15	29	170	48	255	38	51	630
CT alone	2	0	0	1	1	7	2	1	9	9	24	56
Other non-standard	6	21	14	69	55	48	127	22	85	15	13	475
Total	505	952	309	3078	1152	1170	3233	330	2985	332	249	13982

Fig. 3. Carcinoma of the cervix uteri: patients treated in 1996–98. Distribution of patients by stage and treatment.

Table 15
Carcinoma of the cervix uteri: patients treated in 1996-98. Response to treatment by stage

Age at diagnosis	All	Missing	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb
Missing	3439	97	377	92	822	362	248	544	45	669	104	79
Complete response	7316	55	508	181	2019	613	719	1916	124	1092	63	26
Partial response	1408	11	4	11	50	55	76	394	93	620	60	34
Stable disease	431	19	11	2	28	15	17	70	20	184	36	29
Progressive disease	721	4	14	6	40	53	61	162	29	241	53	58
Not assessable	667	6	38	17	119	54	49	147	19	179	16	23
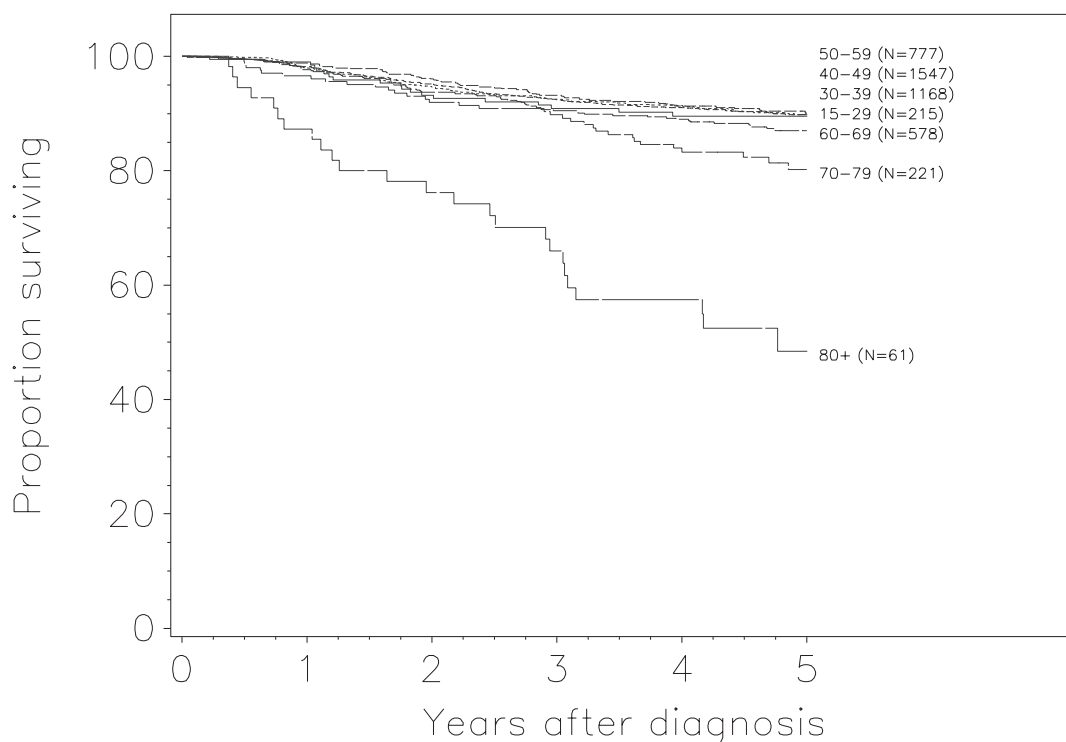
Age group	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
15–29	215	26.8	99.0	93.2	90.9	89.6	89.6	1.0 (0.6–1.7)
30–39	1168	35.1	98.1	94.6	92.5	91.4	89.7	1.1 (0.8–1.4)
40–49	1547	44.3	98.2	95.2	92.4	91.0	89.8	1.0 (0.8–1.4)
50–59	777	54.4	98.8	96.1	93.2	91.3	90.2	Reference
60-69	578	63.9	97.7	93.7	90.5	89.0	87.0	1.3 (0.9–1.9)
70–79	221	73.2	96.7	92.1	89.9	83.8	80.2	1.9 (1.3–2.9)
80+	61	83.0	87.9	76.6	66.4	57.5	48.2	6.4 (4.0–10.3)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for country.

Fig. 4. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by age (Stage I), *n* = 4567.
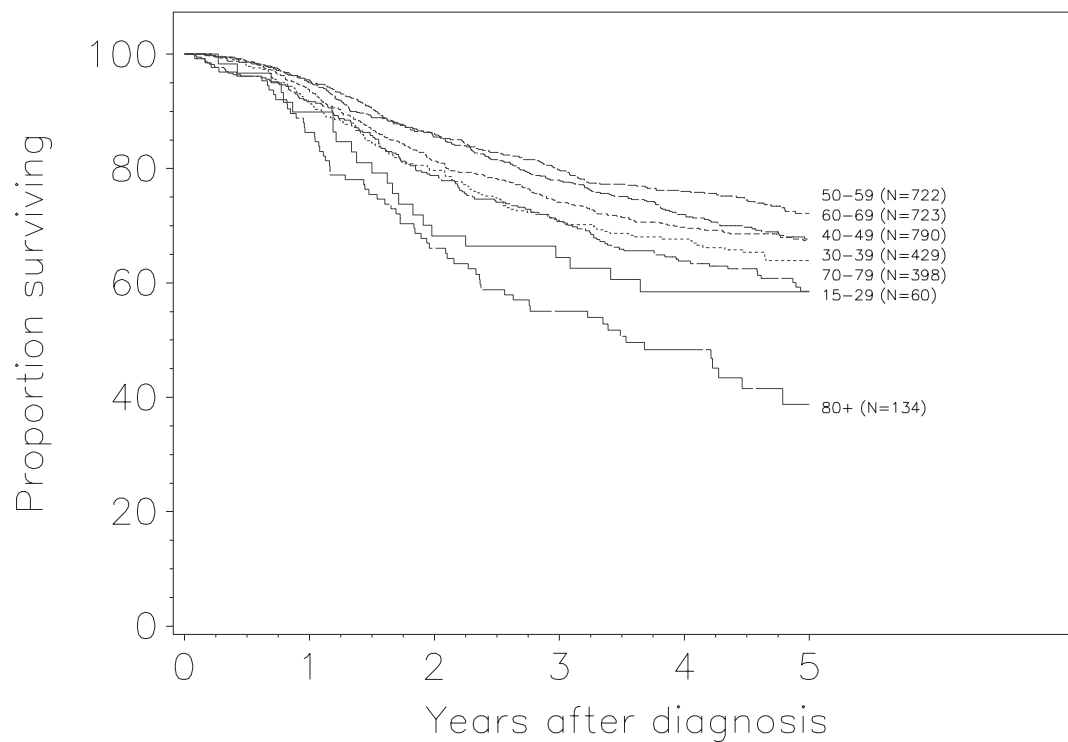
Age group	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
15–29	60	26.9	89.8	68.5	64.7	58.4	58.4	1.5 (1.0–2.3)
30–39	429	35.4	91.5	79.9	70.9	67.7	63.7	1.3 (1.1–1.7)
40–49	790	44.5	93.5	81.5	74.3	69.7	67.4	1.2 (1.0–1.4)
50–59	722	54.5	95.1	86.3	79.9	76.0	72.3	Reference
60-69	723	64.3	95.6	85.6	78.0	71.9	67.6	1.2 (1.0–1.4)
70–79	398	73.5	91.8	78.9	70.9	63.7	59.2	1.4 (1.1–1.8)
80+	134	83.4	86.7	66.4	55.2	48.4	39.8	2.5 (1.9–3.3)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for country.
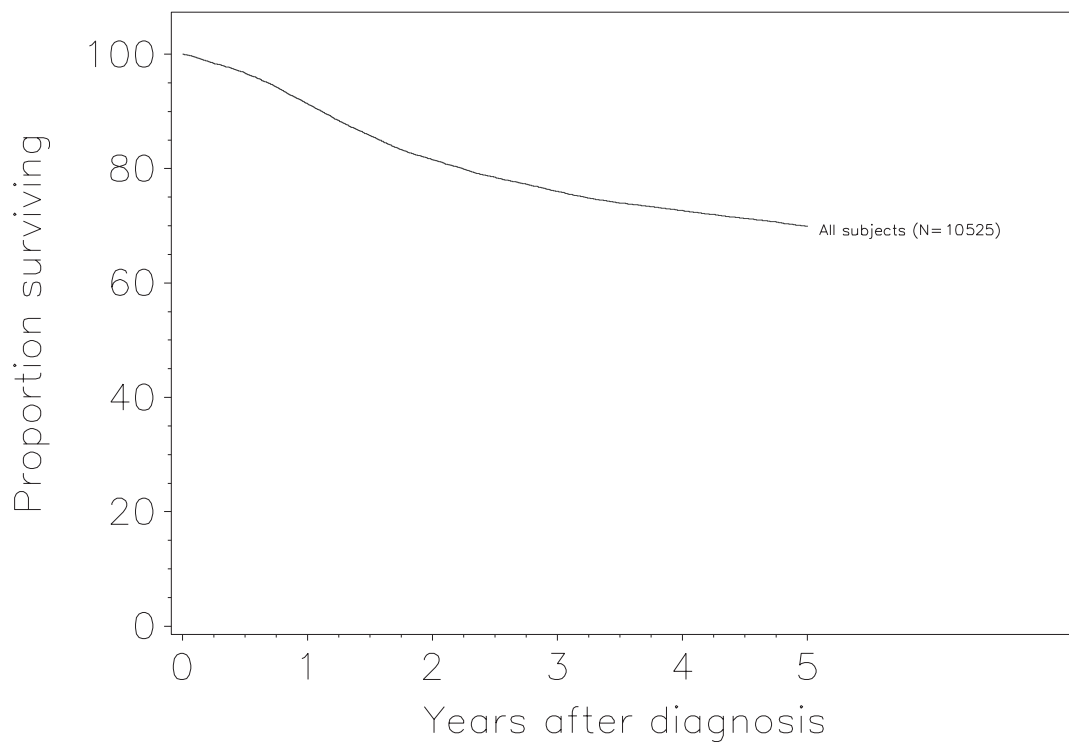
Fig. 5. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by age (Stage II), *n* = 3256.
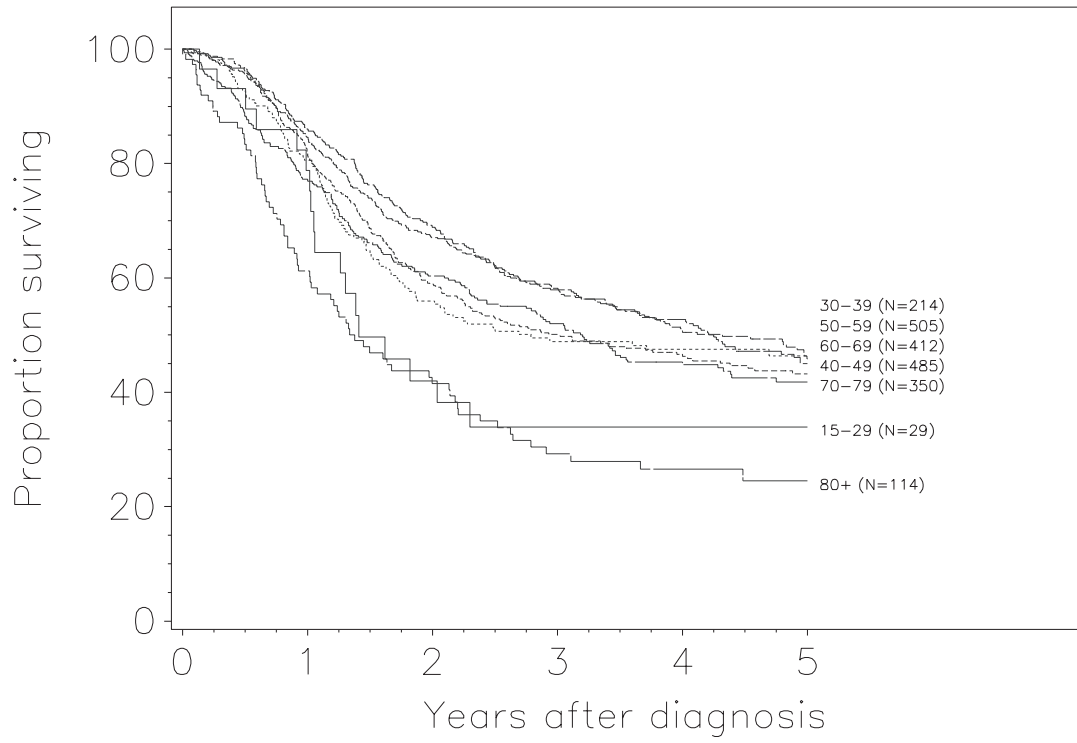
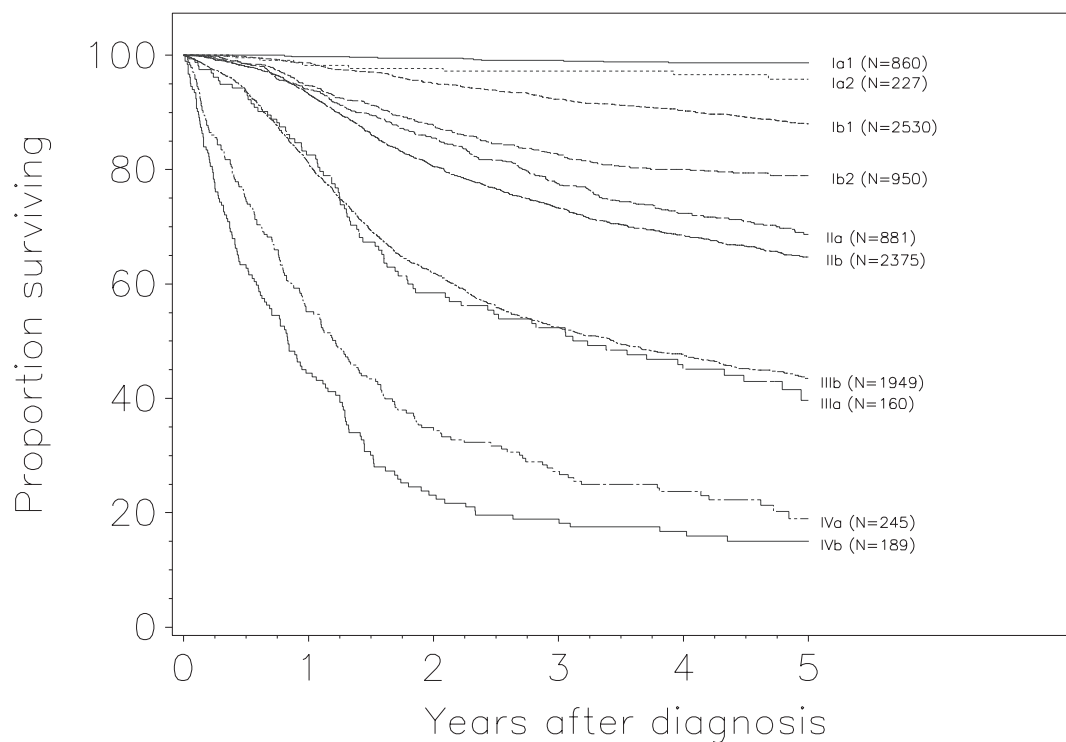| Age group	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
15–29	29	26.6	78.9	42.2	33.8	33.8	33.8	1.6 (1.0–2.6)
30–39	214	35.3	81.1	56.2	49.1	47.7	46.7	1.1 (0.9–1.4)
40–49	485	44.9	82.0	59.4	50.5	46.9	43.2	1.1 (0.9–1.3)
50–59	505	54.6	84.7	67.0	58.0	50.6	46.2	Reference
60–69	412	64.5	86.4	69.2	58.1	52.7	44.9	1.0 (0.8–1.2)
70–79	350	73.9	77.7	60.7	52.2	45.1	41.5	1.2 (1.0–1.4)
80+	114	83.6	62.8	42.6	29.6	26.7	24.5	1.9 (1.5–2.5)

[a] Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for country.

Fig. 6. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by age (Stage III), $n = 2109$.
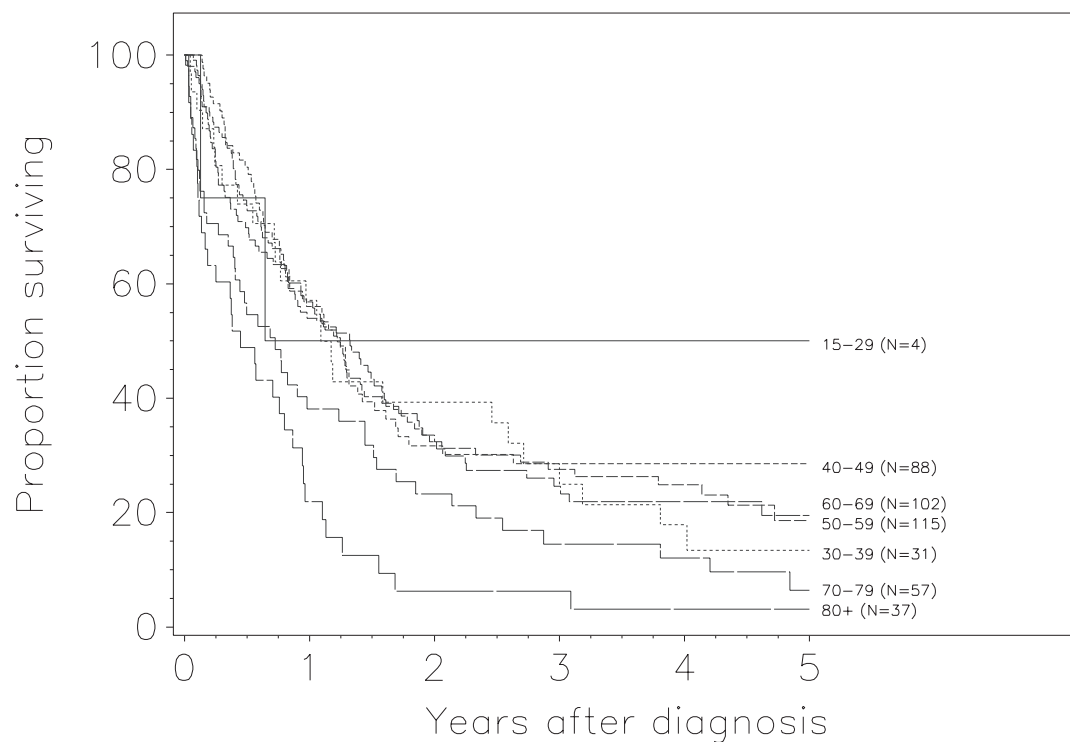
Age group	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
15–29	4	27.3	50.0	50.0	50.0	50.0	50.0	0.5 (0.1–2.2)
30–39	31	35.5	57.4	40.0	29.1	17.5	12.5	1.0 (0.7–1.7)
40–49	88	44.8	57.6	32.8	29.5	29.5	29.5	0.9 (0.6–1.3)
50–59	115	54.9	54.6	32.8	27.9	25.0	18.5	Reference
60–69	102	64.5	57.9	34.5	25.2	22.1	19.5	1.0 (0.7–1.4)
70–79	57	74.2	40.2	24.6	15.2	12.7	7.0	1.4 (0.9–2.0)
80+	37	84.5	23.9	6.8	6.8	3.4	3.4	2.3 (1.5–3.5)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for country.

Fig. 7. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by age (Stage IV), *n* = 434.
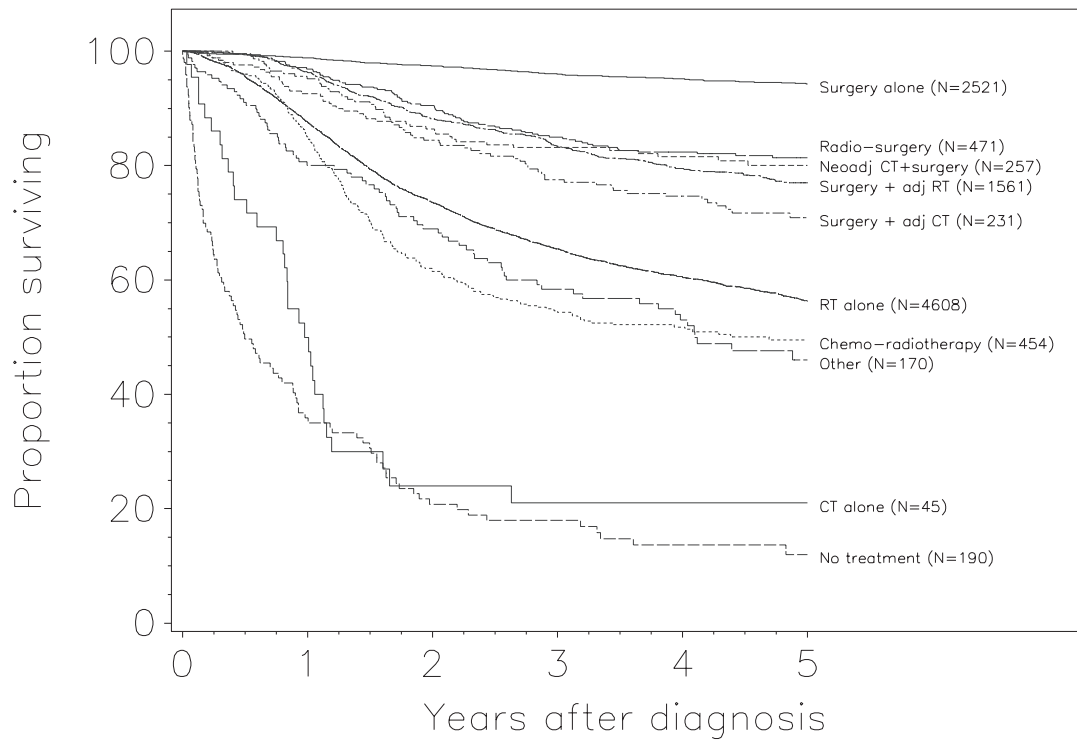
Fig. 8. Carcinoma of the cervix uteri: patients treated in 1996–98. Overall survival, $n = 10525$.

	Patients (n)	Mean age (yr)	Overall survival (%) at				
			1 year	2 years	3 years	4 years	5 years
All subjects	10525	52.0	91.4	81.6	76.1	72.6	69.9

Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio [a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	860	44.3	99.8	99.5	99.1	98.7	98.7	0.1 (0.1–0.2)
Ia2	227	45.5	98.2	97.7	97.2	96.7	95.9	0.3 (0.1–0.5)
Ib1	2530	48.3	98.7	95.1	92.3	90.4	88.0	Reference
Ib2	950	47.4	94.8	87.8	82.6	79.9	78.8	
IIa	881	56.5	94.1	85.6	77.6	72.3	68.8	2.4 (2.1–2.8)
IIb	2375	54.1	93.3	80.7	73.4	68.5	64.7	2.9 (2.6–3.3)
IIIa	160	60.1	82.8	58.8	52.6	45.3	40.4	5.2 (4.0–6.6)
IIIb	1949	56.4	81.5	62.2	52.6	47.6	43.3	5.7 (5.0–6.4)
IVa	245	60.0	56.1	35.6	27.9	24.1	19.5	12.6 (10.5–15.1)
IVb	189	56.6	45.8	23.9	19.6	17.2	15.0	19.2 (15.8–23.4)

[a] Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.
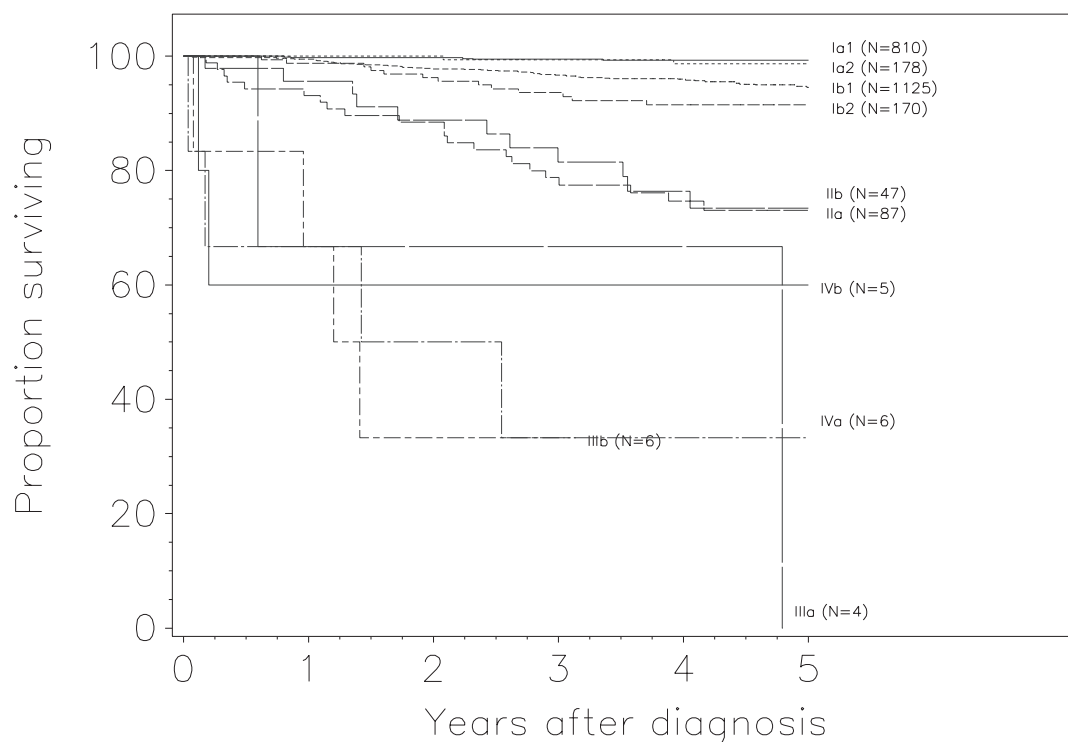
Fig. 9. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage, *n* = 10366.

Fig. 10. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by mode of treatment, $n = 10508$.

Treatment	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
No treatment	190	60.6	48.1	27.6	23.8	17.8	15.9	15.4 (11.5–20.5)
Surgery	2521	45.3	98.8	97.4	96.0	95.1	94.3	Reference
RT alone	4608	57.0	87.8	73.7	65.5	60.6	56.4	3.8 (3.0–4.7)
Radio-surgery	471	46.8	97.0	90.5	85.0	82.3	81.2	2.3 (1.7–3.1)
Neoadj CT + surgery	257	47.4	92.7	86.5	83.2	81.5	80.0	2.9 (2.0–4.1)
Surgery + adj RT	1561	50.1	96.4	88.3	83.5	79.5	76.9	2.7 (2.2–3.4)
Surgery + adj CT	231	47.4	95.2	84.5	77.6	74.7	70.8	3.0 (2.2–4.2)
Chemo-radiotheraphy	454	51.3	85.1	61.7	54.7	51.6	49.1	3.4 (2.7–4.4)
Chemotherapy	45	54.3	51.2	24.2	21.0	21.0	21.0	5.3 (3.5–8.2)
Other	170	50.5	80.0	69.3	58.7	53.3	45.7	4.2 (3.1–5.7)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age, FIGO stage and country.

Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	810	43.9	99.7	99.7	99.5	99.3	99.3	0.2 (0.1–0.4)
Ia2	178	43.6	100.0	100.0	99.4	98.7	98.7	0.3 (0.1–1.0)
Ib1	1125	45.4	99.5	97.8	96.7	95.9	94.5 }	Reference
Ib2	170	45.7	98.8	96.3	93.6	91.4	91.4 }	
IIa	87	54.4	93.1	88.4	78.5	74.4	72.6	4.4 (2.6–7.6)
IIb	47	51.5	95.7	88.8	81.6	76.4	73.0	5.9 (2.9–12.1)
IIIa	4	62.8	71.4	71.4	71.4	71.4	–	7.3 (1.6–34.0)
IIIb	6	60.3	66.7	33.3	33.3	–	–	16.0 (5.4–47.3)
IVa	6	61.3	66.7	50.0	33.3	33.3	33.3	9.2 (3.1–27.6)
IVb	5	59.2	50.0	50.0	50.0	50.0	50.0	16.1 (3.5–73.5)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 11. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (surgery alone), *n* = 2438.
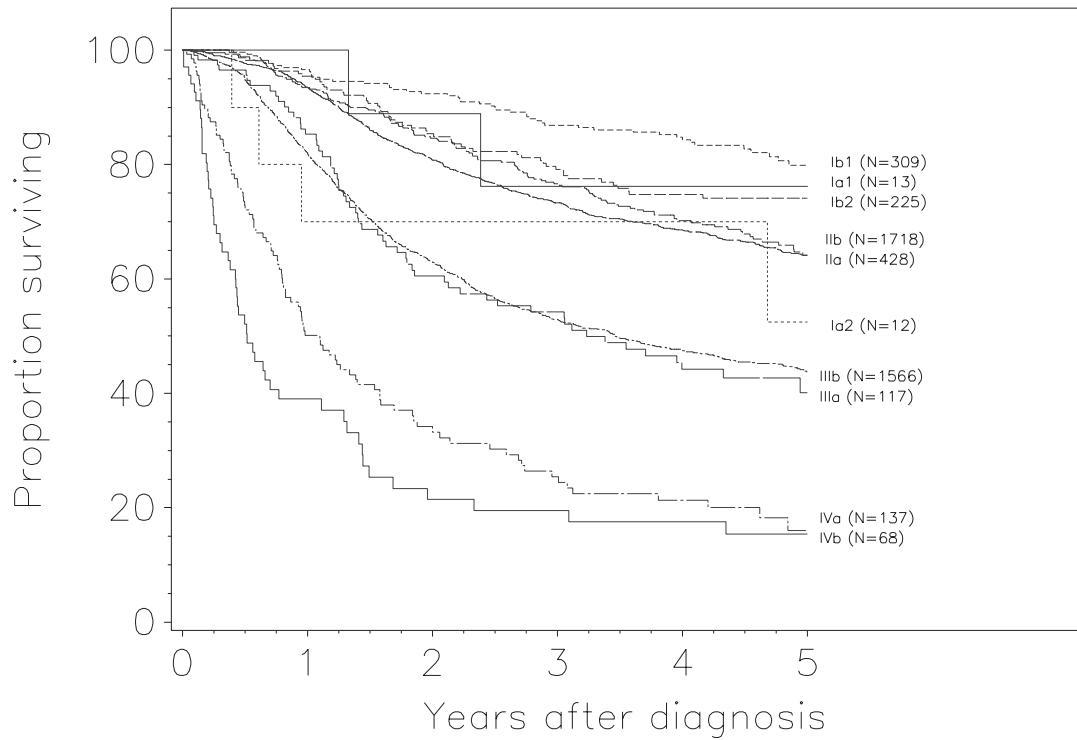
Stage	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	13	61.5	100.0	88.9	76.2	76.2	76.2	1.1 (0.3–4.6)
Ia2	12	62.8	72.7	72.7	72.7	72.7	48.5	1.5 (0.6–4.2)
Ib1	309	59.4	96.7	92.5	86.9	84.8	80.1	Reference
Ib2	225	50.4	95.4	85.2	79.0	74.5	73.7	
IIa	428	60.9	93.6	84.8	76.8	70.2	64.5	1.8 (1.4–2.3)
IIb	1718	55.3	93.5	81.0	73.3	68.5	64.2	1.9 (1.6–2.4)
IIIa	117	63.1	85.6	60.7	54.4	44.3	40.9	3.3 (2.4–4.5)
IIIb	1566	57.2	82.4	63.2	53.1	47.8	43.7	3.7 (3.0–4.5)
IVa	137	61.5	51.0	34.7	25.8	21.5	16.7	8.9 (6.8–11.8)
IVb	68	59.6	38.6	21.2	19.3	17.4	14.5	15.8 (11.2–22.4)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 12. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (radiotherapy), $n = 4593$.
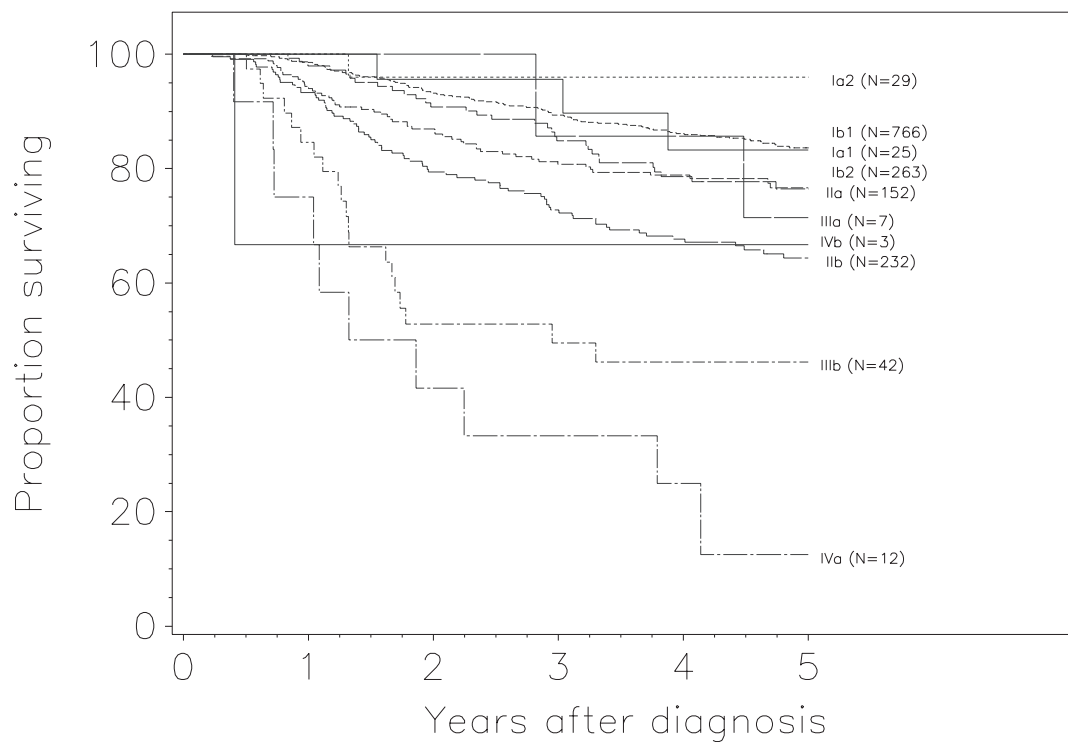
Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	25	50.3	100.0	95.8	95.8	83.5	83.5	0.7 (0.2–2.1)
Ia2	29	50.5	100.0	96.1	96.1	96.1	96.1	0.3 (0.0–1.8)
Ib1	766	49.0	98.7	93.2	89.4	86.1	83.6 }	Reference
Ib2	263	48.9	94.5	87.0	80.8	78.8	76.7	
IIa	152	52.2	98.0	90.9	85.0	78.5	76.2	1.3 (0.9–1.9)
IIb	232	52.2	93.4	79.5	72.8	67.7	64.3	2.0 (1.5–2.7)
IIIa	7	55.7	100.0	100.0	85.7	85.7	70.1	0.7 (0.2–3.1)
IIIb	42	49.4	85.2	52.2	49.0	45.0	45.0	4.4 (2.6–7.3)
IVa	12	57.5	75.0	41.7	33.3	23.8	11.9	7.1 (3.6–14.3)
IVb	3	53.3	66.7	66.7	66.7	66.7	66.7	2.8 (0.3–22.3)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 13. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (surgery + adj RT), *n* = 1531.
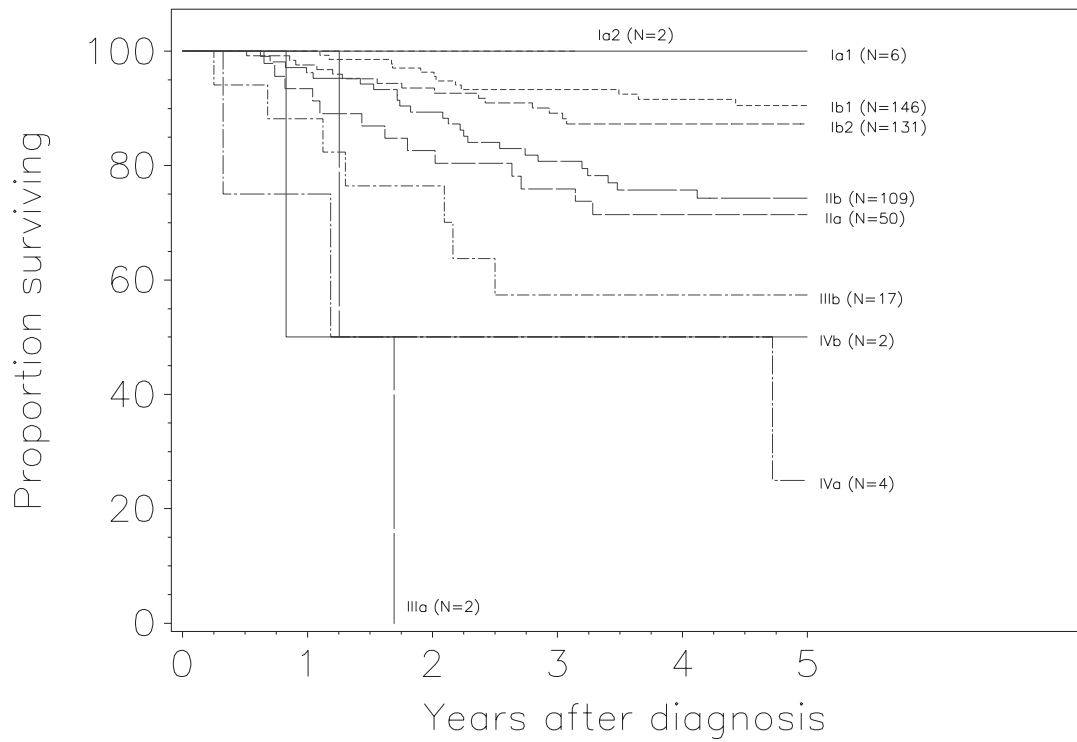
Stage	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	6	48.0	100.0	100.0	100.0	100.0	100.0	–
Ia2	2	47.5	100.0	100.0	100.0	–	–	–
Ib1	146	46.6	100.0	96.4	93.3	91.6	90.4	Reference
Ib2	131	43.9	97.6	93.5	89.1	87.2	87.2	
IIa	50	52.2	93.8	82.8	76.2	71.5	71.5	3.3 (1.6–6.8)
IIb	109	47.2	96.3	89.3	80.7	75.7	73.9	3.3 (1.7–6.3)
IIIa	2	60.0	100.0	–	–	–	–	80.6 (12.6–515)
IIIb	17	51.8	88.2	76.1	55.3	55.3	55.3	4.9 (1.8–13.6)
IVa	4	43.5	75.0	50.0	50.0	50.0	25.0	8.1 (1.7–38.1)
IVb	2	41.5	50.0	50.0	50.0	50.0	50.0	13.3 (1.1–155)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.
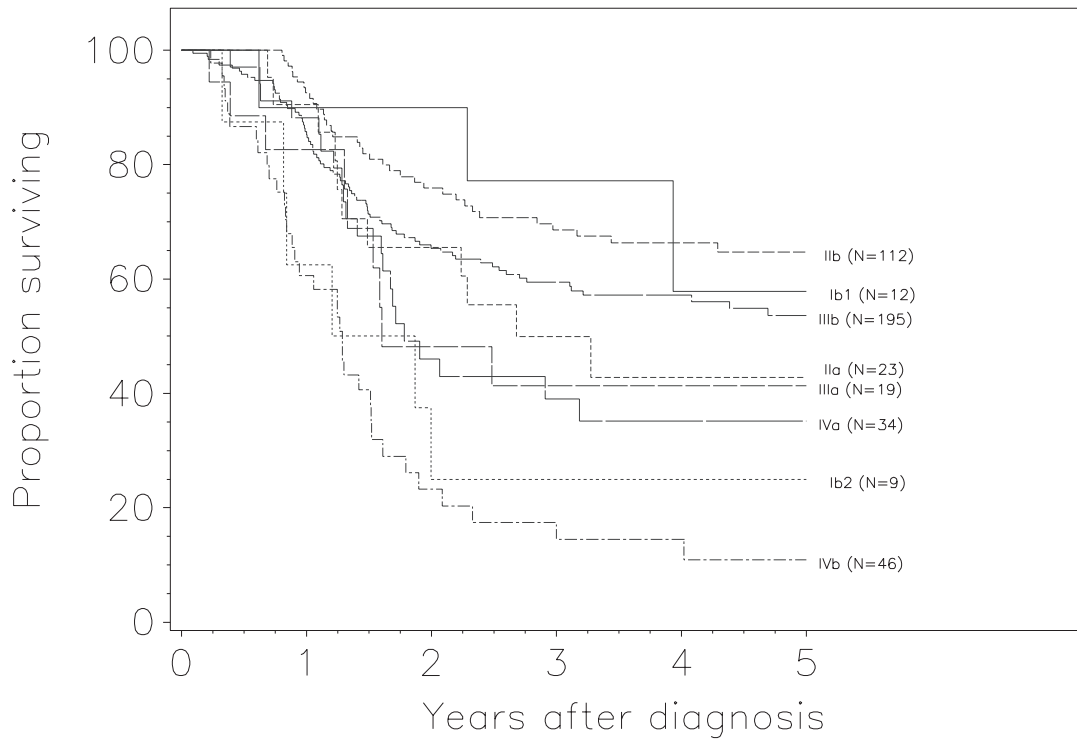
Fig. 14. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (radio-surgery), n = 469.
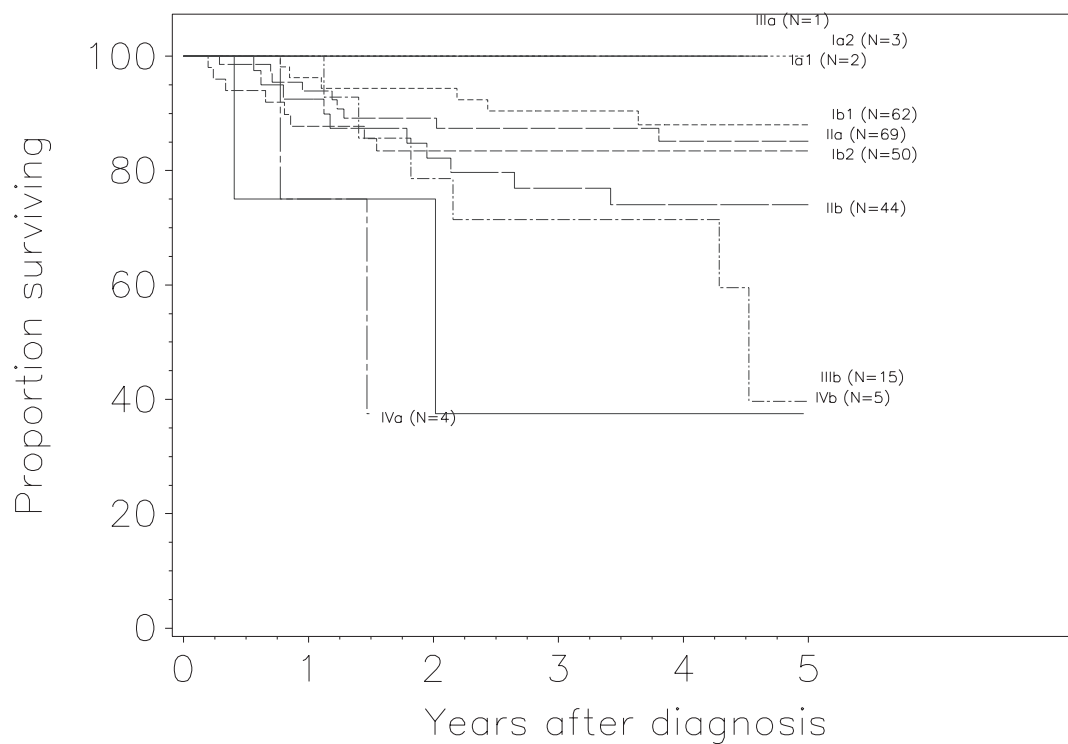
Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	2	51.5	100.0	100.0	100.0	100.0	–	–
Ia2	3	46.0	100.0	100.0	100.0	100.0	100.0	–
Ib1	62	48.1	96.5	94.6	90.5	88.0	88.0	Reference
Ib2	50	42.6	87.6	83.4	83.4	83.4	83.4	
IIa	69	49.0	94.0	89.1	87.2	85.0	85.0	1.4 (0.6–3.5)
IIb	44	48.3	92.9	82.7	77.3	74.2	74.2	1.4 (0.5–4.2)
IIIa	1	35.0	100.0	100.0	100.0	100.0	–	–
IIIb	15	50.7	100.0	78.6	70.7	70.7	45.0	1.8 (0.5–7.4)
IVa	4	49.5	75.0	–	–	–	–	6.0 (0.9–38.5)
IVb	5	48.6	77.8	77.8	38.9	38.9	–	3.7 (0.2–60.4)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 15. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (CT + surgery), *n* = 255.

Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	0	–	–	–	–	–	–	–
Ia2	0	–	–	–	–	–	–	–
Ib1	12	52.3	90.0	90.0	76.2	59.2	59.2	Reference
Ib2	9	51.2	64.7	25.9	25.9	25.9	25.9	
IIa	23	55.1	90.9	66.3	50.4	43.2	43.2	1.4 (0.5–3.5)
IIb	112	50.9	92.7	76.1	68.7	66.2	64.4	0.6 (0.3–1.2)
IIIa	19	45.1	82.9	49.7	42.6	42.6	42.6	1.6 (0.6–4.3)
IIIb	195	50.9	85.5	65.3	59.3	56.7	52.8	1.0 (0.5–2.0)
IVa	34	52.5	88.2	46.4	39.5	35.5	35.5	1.1 (0.5–2.6)
IVb	46	52.1	61.4	24.8	18.6	15.2	10.9	3.0 (1.4–6.6)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 16. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (chemo-radiotherapy), *n* = 450.
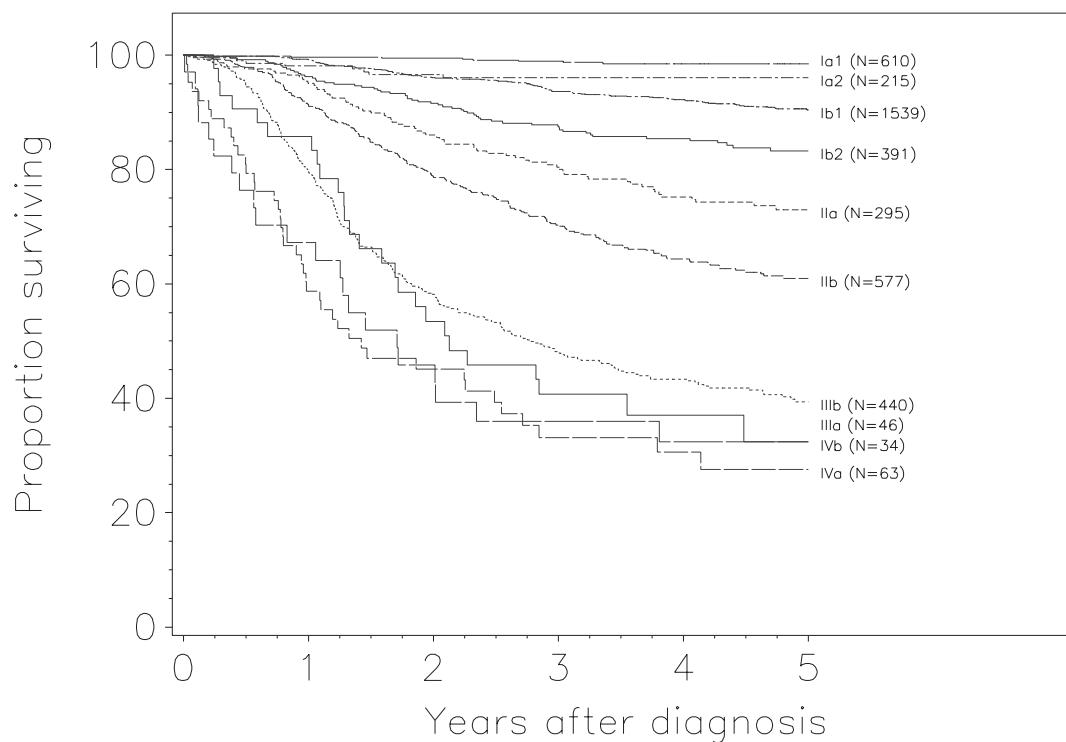
pT (UICC-TNM)	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio [a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
pT Ia1	610	44.5	99.7	99.5	98.9	98.5	98.5	0.2 (0.1–0.4)
pT Ia2	215	45.8	98.1	96.6	96.1	96.1	96.1	0.4 (0.2–0.8)
pT Ib1	1539	47.6	99.2	96.1	93.7	92.3	90.4 }	Reference
pT Ib2	391	46.9	96.3	91.6	87.6	85.3	83.1	
pT IIa	295	53.6	95.1	86.1	80.5	75.2	72.8	2.7 (2.1–3.6)
pT IIb	577	51.9	91.2	79.0	70.2	64.4	60.9	3.4 (2.8–4.3)
pT IIIa	46	56.5	86.2	53.7	40.9	37.8	32.4	6.2 (4.0–9.5)
pT IIIb	440	51.9	80.0	58.3	48.3	43.4	39.5	6.6 (5.4–8.2)
pT IVa	63	58.7	58.7	44.9	32.7	30.2	25.8	11.3 (8.0–16.1)
pT IVb	34	51.9	67.2	45.3	35.2	31.7	31.7	9.5 (6.0–14.9)

[a] Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 17. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by pT(UICC-TNM), *n* = 4210.
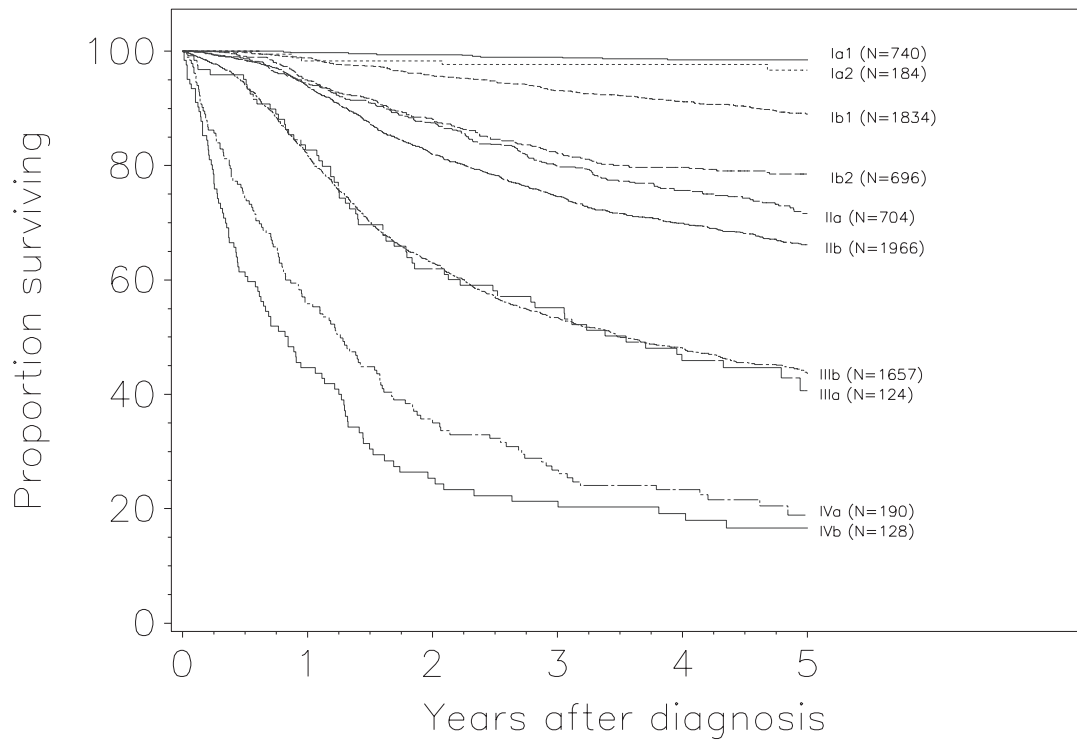
Stage	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	740	44.4	99.7	99.4	99.0	98.5	98.5	0.1 (0.1–0.2)
Ia2	184	45.3	98.3	98.3	97.7	97.7	96.8	0.2 (0.1–0.6)
Ib1	1834	48.8	98.9	95.7	93.2	91.2	89.1	Reference
Ib2	696	47.2	95.1	88.1	82.2	79.6	78.4	
IIa	704	56.9	94.3	87.5	80.0	75.6	71.8	2.3 (1.9–2.8)
IIb	1966	54.0	93.9	82.1	74.7	69.9	66.2	2.9 (2.5–3.3)
IIIa	124	61.1	83.0	62.4	55.5	46.1	41.7	5.4 (4.1–7.1)
IIIb	1657	56.3	82.3	63.2	53.5	48.1	43.6	5.9 (5.2–6.8)
IVa	190	59.7	57.0	36.7	27.6	23.9	19.6	13.8 (11.2–17.0)
IVb	128	55.6	46.1	26.2	22.0	19.8	16.6	20.2 (15.9–25.6)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 18. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (epidermoid), $n = 8223$.
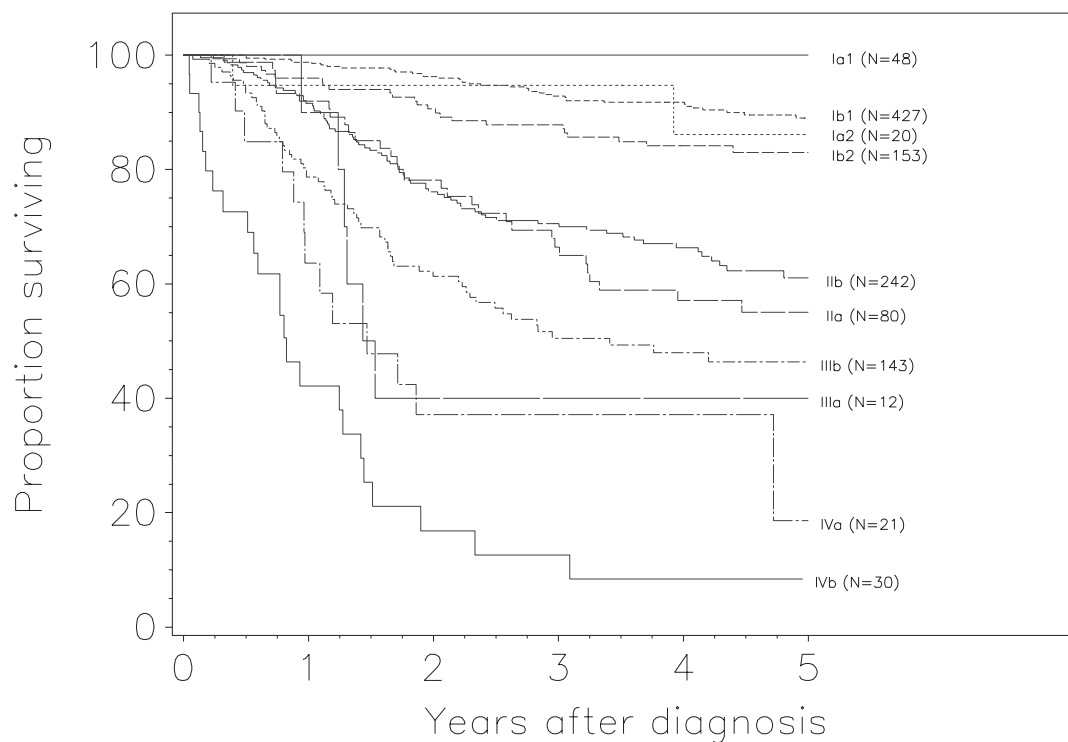
Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	48	43.6	100.0	100.0	100.0	100.0	100.0	–
Ia2	20	49.2	94.9	94.9	94.9	88.1	88.1	1.0 (0.2–4.2)
Ib1	427	46.6	98.8	96.3	92.9	91.7	88.7 }	Reference
Ib2	153	48.4	96.0	90.6	87.8	83.9	82.8 }	
IIa	80	54.4	92.2	78.3	66.7	57.2	54.9	3.9 (2.5–6.0)
IIb	242	54.7	91.8	76.4	70.7	66.4	61.0	4.1 (2.8–6.0)
IIIa	12	57.0	90.9	40.4	40.4	40.4	40.4	6.7 (2.8–16.1)
IIIb	143	57.8	79.4	61.9	51.0	48.4	46.6	6.7 (4.5–10.0)
IVa	21	60.5	65.0	37.9	37.9	37.9	22.8	9.1 (4.8–17.5)
IVb	30	60.8	42.9	17.1	12.9	7.7	–	23.1 (13.5–39.7)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 19. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (adenocarcinoma), *n* = 1176.
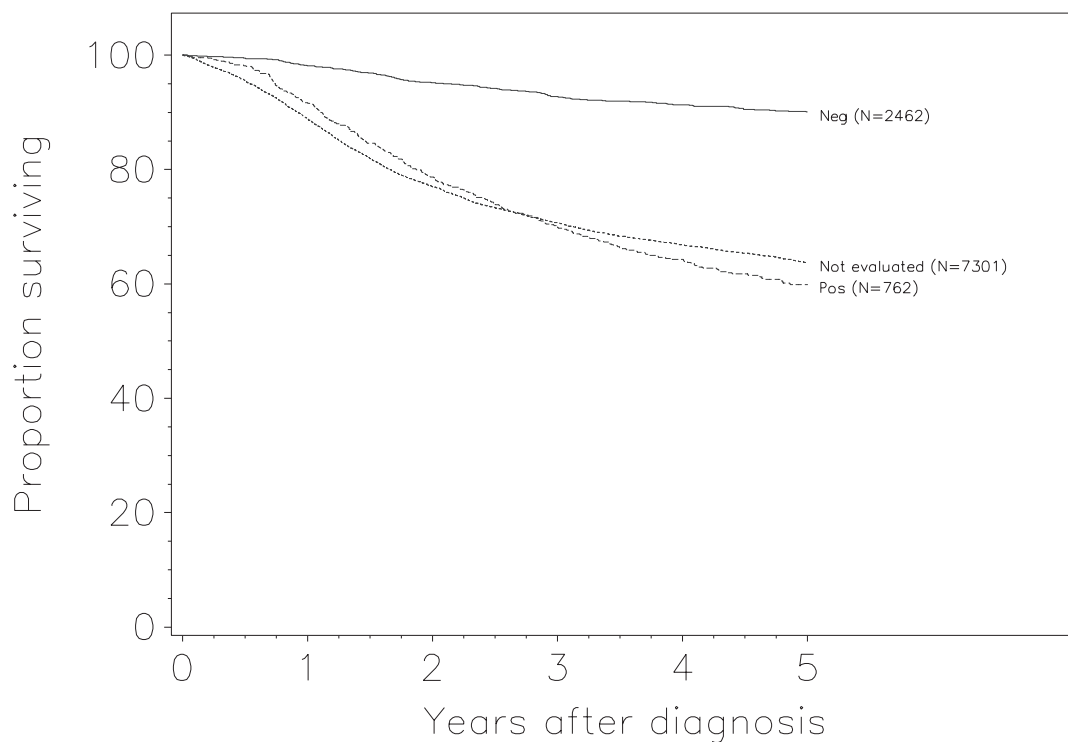
Lymph nodes	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Negative	2462	46.9	98.2	95.2	92.8	91.3	90.0	Reference
Positive	762	47.9	91.8	78.8	70.0	64.2	59.5	3.1 (2.6–3.8)
Unknown	7301	54.1	89.0	77.2	70.8	66.9	63.8	2.3 (1.9–2.7)

[a] Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age, FIGO stage and country.

Fig. 20. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by lymphnodal status, *n* = 10525.
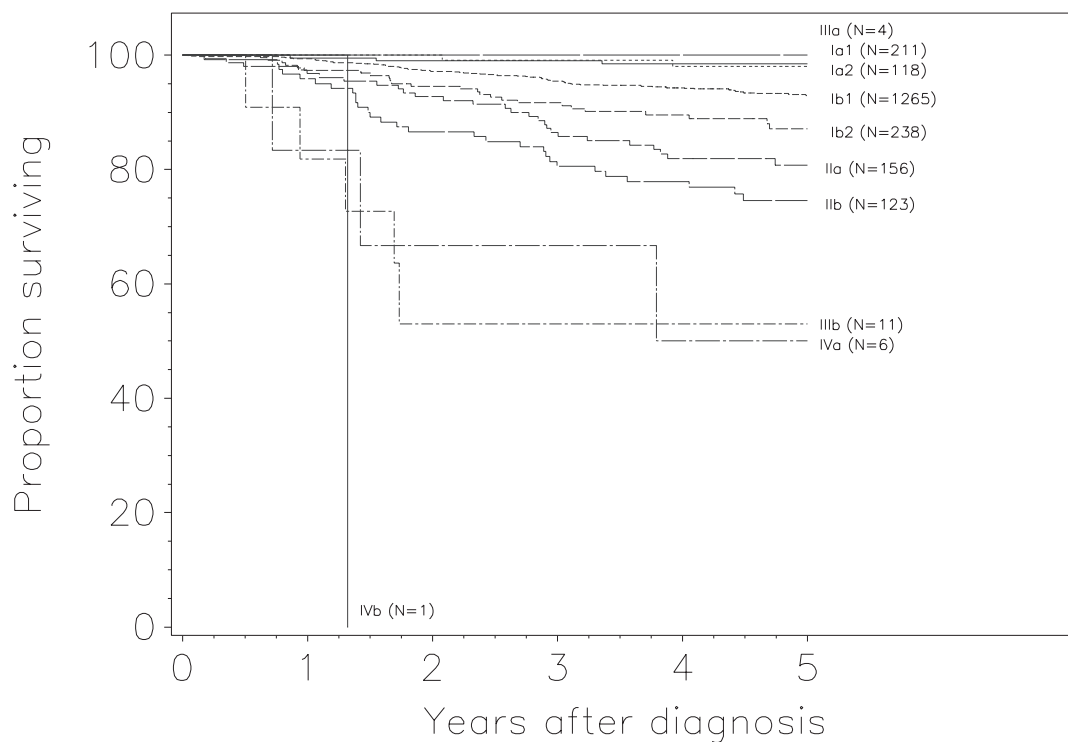
Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	211	44.2	99.5	99.0	99.0	98.4	98.4	0.2 (0.1–0.7)
Ia2	118	43.5	100.0	100.0	99.1	98.1	98.1	0.3 (0.1–0.9)
Ib1	1265	45.9	99.4	97.2	95.4	94.3	92.9	Reference
Ib2	238	47.3	97.4	94.7	91.7	89.5	87.1	
IIa	156	53.3	96.8	92.7	86.5	81.9	80.9	2.5 (1.6–3.9)
IIb	123	53.1	95.9	86.6	80.6	77.9	74.4	3.0 (1.8–4.8)
IIIa	4	54.8	100.0	100.0	100.0	100.0	100.0	–
IIIb	11	43.7	81.8	52.9	52.9	52.9	52.9	10.4 (3.5–30.8)
IVa	6	48.7	83.3	66.7	66.7	50.0	50.0	6.3 (2.0–20.2)
IVb	1	68.0	100.0	–	–	–	–	17.4 (0.9–345)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.
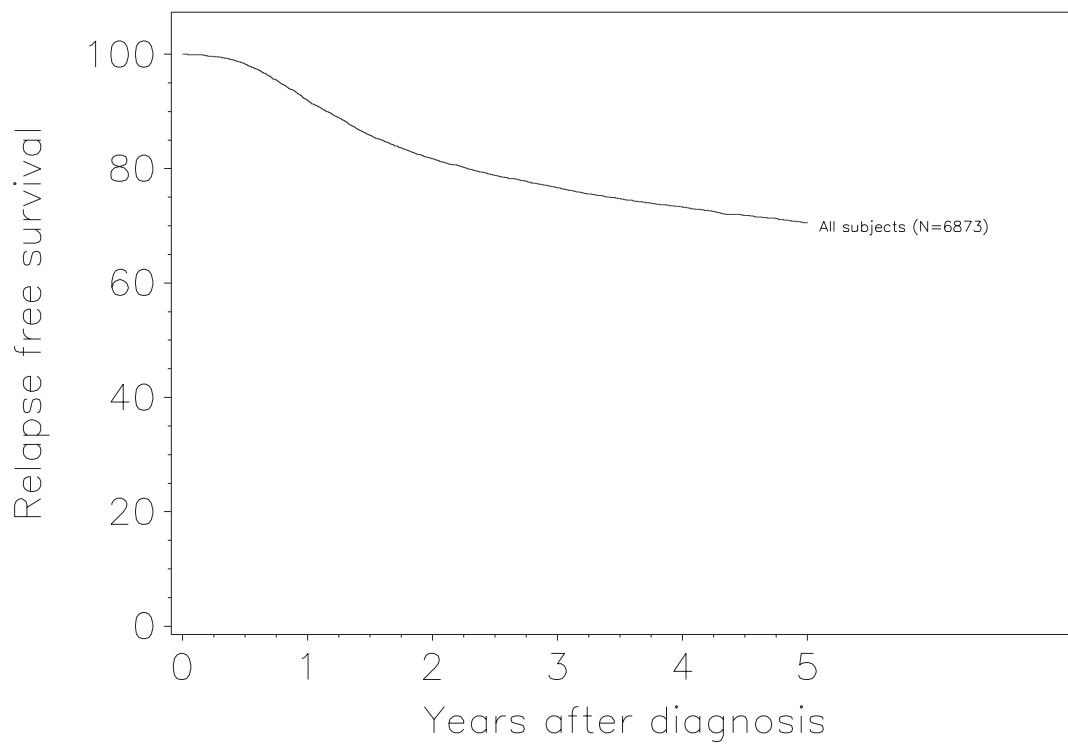
Fig. 21. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (upfront surgery, negative node), *n* = 2133.
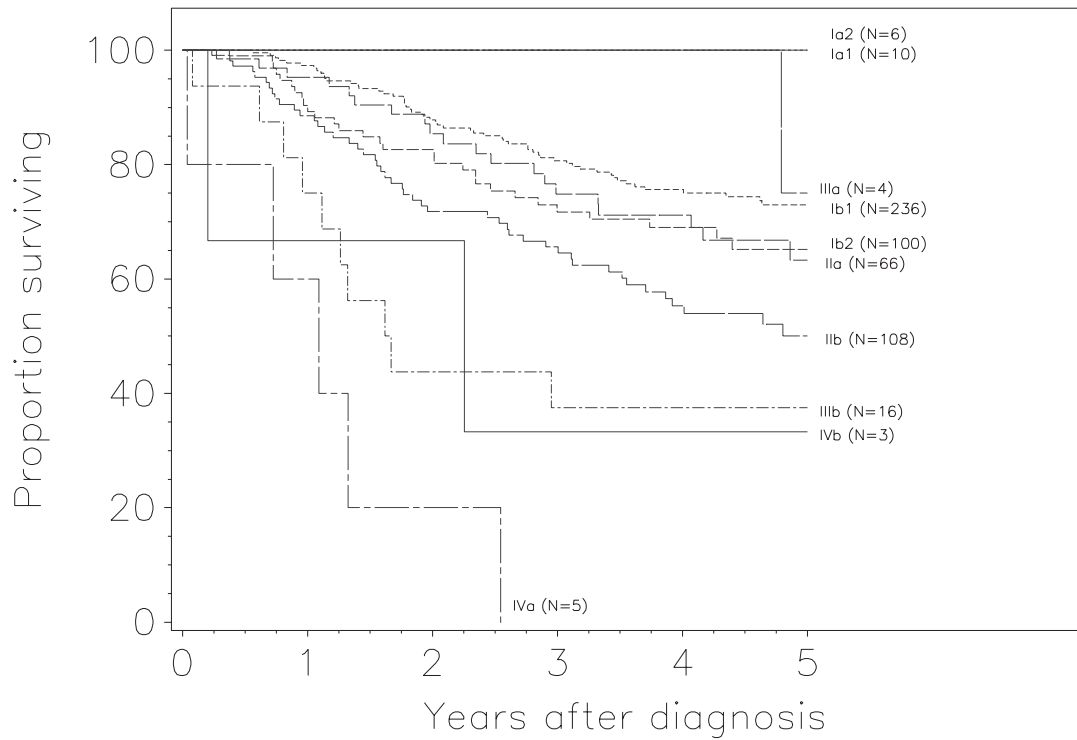
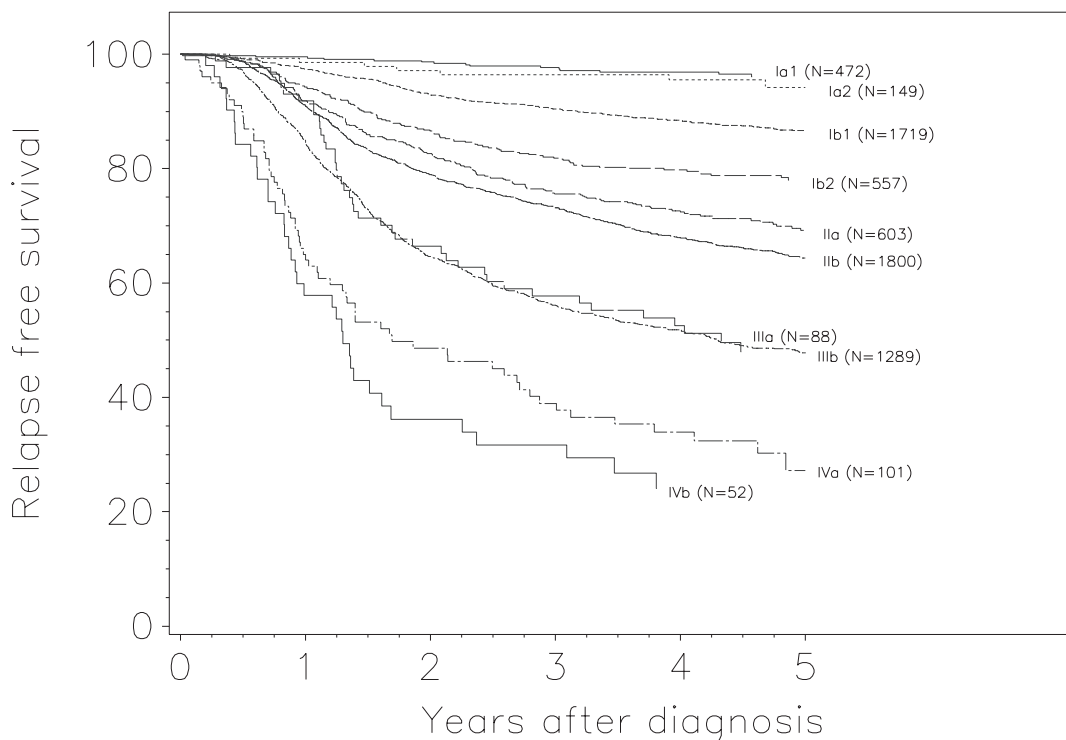| Stage	Patients (*n*)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	10	48.0	100.0	100.0	100.0	100.0	100.0	–
Ia2	6	43.5	100.0	100.0	100.0	100.0	100.0	–
Ib1	236	46.0	97.4	87.9	80.8	75.5	72.7	Reference
Ib2	100	44.7	90.6	82.7	71.8	69.0	65.0	
IIa	66	50.7	95.3	85.5	75.0	71.1	62.8	1.4 (0.9–2.4)
IIb	108	51.4	88.6	71.9	65.7	55.3	50.5	2.1 (1.4–3.3)
IIIa	4	55.5	100.0	100.0	100.0	100.0	75.0	0.6 (0.1–4.3)
IIIb	16	50.9	75.0	43.8	37.5	37.5	37.5	3.7 (1.7–8.2)
IVa	5	63.2	60.0	20.0	–	–	–	11.7 (4.2–32.6)
IVb	3	51.7	66.7	66.7	33.3	33.3	33.3	5.9 (1.1–32.3)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 22. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage (upfront surgery, positive node), *n* = 554.

Fig. 23. Carcinoma of the cervix uteri: patients treated in 1996–98. Relapse-free survival, *n* = 6873.

	Patients (*n*)	Mean age (yr)	Relapse-free survival (%) at				
			1 year	2 years	3 years	4 years	5 years
All subjects	6873	51.9	92.0	81.8	76.7	73.3	70.5

Stage	Patients (*n*)	Mean age (yr)	Relapse-free survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	472	44.3	99.6	98.6	97.6	96.8	96.0	0.2 (0.1–0.4)
Ia2	149	45.3	98.6	97.2	96.5	95.6	94.4	0.3 (0.2–0.7)
Ib1	1719	48.8	97.4	92.9	90.4	88.4	86.5	Reference
Ib2	557	47.3	94.3	86.6	81.9	79.7	77.9	
IIa	603	57.1	91.9	82.7	75.6	72.6	69.2	2.2 (1.9–2.7)
IIb	1800	53.7	91.1	79.1	73.3	67.9	64.4	2.6 (2.3–3.1)
IIIa	88	62.3	91.9	66.7	58.0	52.7	47.1	3.9 (2.8–5.4)
IIIb	1289	56.0	84.8	64.8	56.3	51.8	47.5	4.6 (4.0–5.4)
IVa	101	56.8	64.5	48.9	39.2	33.8	27.7	8.1 (6.2–10.6)
IVb	52	56.2	58.4	36.8	32.2	24.8	24.8	10.3 (7.2–14.7)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 24. Carcinoma of the cervix uteri: patients treated in 1996–98. Relapse-free survival by FIGO stage, *n* = 6830.
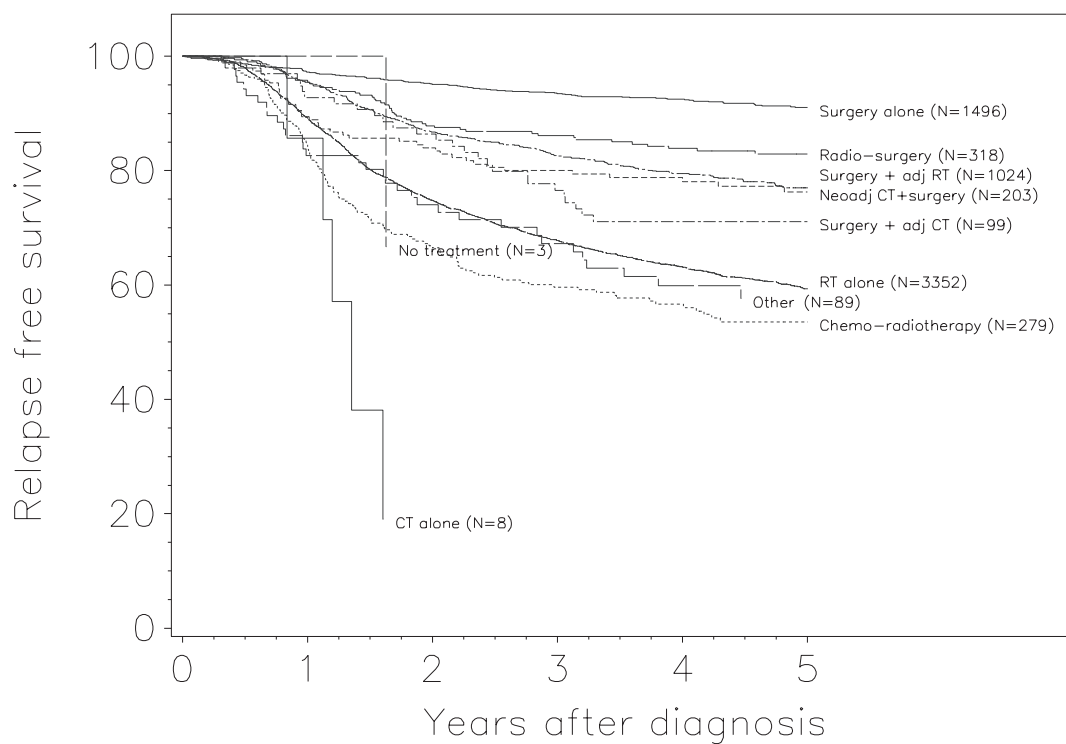
Treatment	Patients (*n*)	Mean age (yr)	Relapse-free survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
No treatment	3	46.3	100.0	66.7	66.7	66.7	66.7	2.0 (0.3–14.5)
Surgery	1496	45.3	97.3	95.1	93.5	92.4	90.9	Reference
RT alone	3352	56.4	89.3	74.9	67.9	63.2	59.3	2.0 (1.5–2.5)
Radio-surgery	318	46.5	95.5	87.9	86.2	83.9	82.9	1.2 (0.8–1.7)
Neoadj CT + surgery	203	47.4	89.7	84.2	80.2	78.9	76.3	1.9 (1.3–2.7)
Surgery + adj RT	1024	51.0	95.5	86.8	82.7	79.5	76.9	1.5 (1.2–1.9)
Surgery + adj CT	99	47.8	92.8	86.5	76.8	71.0	71.0	1.8 (1.2–2.8)
Chemo-radiotheraphy	279	51.1	84.2	66.6	59.5	56.6	52.9	2.1 (1.5–2.8)
Chemotherapy	8	53.0	86.7	23.6	23.6	23.6	23.6	4.5 (1.8–11.4)
Other	89	46.8	82.9	74.4	67.7	59.9	57.6	2.0 (1.3–3.0)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age, FIGO stage and country.

Fig. 25. Carcinoma of the cervix uteri: patients treated in 1996–98. Relapse-free survival by treatment age, *n* = 6871.
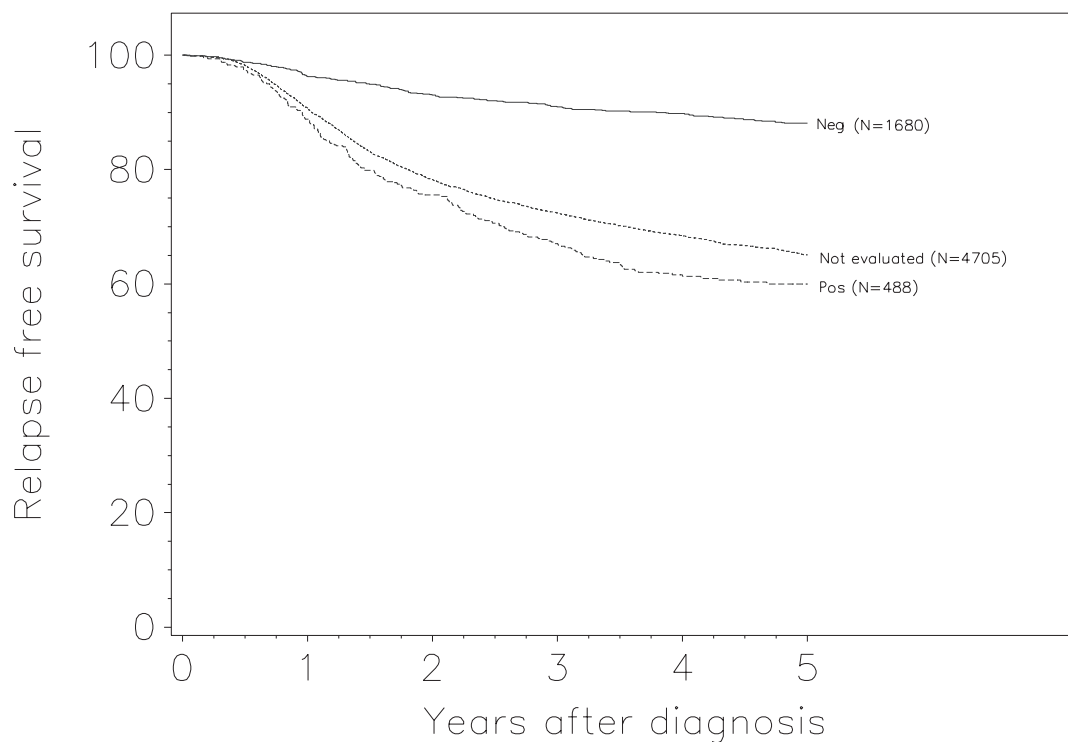
Lymph nodes	Patients (*n*)	Mean age (yr)	Relapse-free survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Negative	1680	47.1	96.3	93.1	91.0	89.8	88.0	Reference
Positive	488	49.2	88.9	75.6	67.0	61.4	59.7	2.7 (2.2–3.4)
Unknown	4705	54.0	90.8	78.3	72.5	68.5	65.1	1.9 (1.6–2.3)

[a] Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age, FIGO stage and country.

Fig. 26. Carcinoma of the cervix uteri: patients treated in 1996–98. Relapse-free survival by lymphnodal status, *n* = 6873.

Table 16
Carcinoma of the cervix uteri: patients treated in 1996–98. Multivariate analysis

Strata	Hazards ratios (95% CI)[a]			
	Stage I	Stage II	Stage III	Stage IV
Age				
Aged<50	Reference	Reference	Reference	Reference
Aged 50+	1.29 (1.07–1.56)	0.97 (0.85–1.11)	0.97 (0.85–1.11)	1.04 (0.79–1.38)
Histologic type				
No/biopsy negative	2.47 (1.13–5.38)	0.79 (0.32–1.95)	0.98 (0.52–1.83)	3.17 (1.31–7.68)
Epidermoid	Reference	Reference	Reference	Reference
Adenocarcinoma	1.29 (0.98–1.70)	1.37 (1.11–1.69)	1.13 (0.88–1.44)	0.85 (0.59–1.24)
Adenosquamous carcinoma	1.29 (0.86–1.93)	1.16 (0.84–1.60)	1.25 (0.88–1.77)	1.09 (0.61–1.95)
Clear cell carcinoma	3.17 (0.78–13.0)	1.86 (0.92–3.79)	2.08 (0.82–5.25)	1.98 (0.60–6.58)
Other	2.39 (1.59–3.60)	1.45 (1.01–2.09)	1.09 (0.74–1.61)	0.79 (0.48–1.29)
Grade				
Grade 1	Reference	Reference	Reference	Reference
Grade 2	2.75 (1.86–4.06)	1.27 (1.00–1.61)	1.47 (1.14–1.89)	1.35 (0.86–2.13)
Grade 3	3.78 (2.54–5.62)	1.34 (1.05–1.72)	1.48 (1.14–1.92)	1.67 (1.06–2.63)
Grade unknown	1.87 (1.26–2.77)	1.33 (1.05–1.69)	1.52 (1.17–1.96)	1.60 (1.01–2.53)
Tumor size				
<4cm	Reference	Reference	Reference	Reference
>4cm	2.02 (1.23–3.34)	1.73 (1.46–2.03)	2.12 (1.74–2.59)	1.54 (1.00–2.37)
Unknown tumor size	1.05 (0.51–2.19)	1.83 (1.46–2.28)	2.28 (1.72–3.01)	1.63 (0.96–2.76)
Lymphnodal status				
Negative	Reference	Reference	Reference	Reference
Positive	4.20 (3.23–5.47)	2.51 (1.85–3.40)	2.74 (1.45–5.18)	2.20 (0.87–5.54)
Unknown	1.83 (1.42–2.36)	2.23 (1.69–2.95)	2.14 (1.25–3.68)	3.96 (1.88–8.37)

[a]From Cox proportional hazard regression model, also adjusted for country.