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Queensland Centre for Gynaecological Cancer

Outcome data statistical report 2008

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Foreword

It gives me great pleasure to present this statistical report which represents a quarter of a century of data collection, from 1982 until 2007, from the Queensland Centre for Gynaecological Cancer (QCGC), located at Royal Brisbane and Women's Hospital and Mater Hospital, Brisbane, Australia.

The centre started in 1982 as the Gynaecological Cancer Unit at Royal Women's Hospital, Brisbane, providing services to women with genital tract cancer who were referred to the hospital. Its first director of services was Dr MJ Webb who had moved from the Mayo Clinic in Rochester, USA, in the early 1980s.

In 1993, following my appointment as the new Director of Gynaecological Oncology, the QCGC was established as the centre responsible to Queensland Health for the provision of gynaecological cancer services in the state of Queensland.

Over the last 14 years the centre has grown from a fledgling clinical service with one certified gynaecological oncologist and one clinical fellow, to the largest such service in Australia with six certified gynaecological oncologists, three clinical fellows, and at least one research fellow, and seeing over 2000 new patients a year (92 percent of Queensland's gynaecological cancer cases).

The centre now runs active training, teaching and research programs that attract trainee applications from within Australia and all around the world.

To date we have had trainees from the United Kingdom, Europe, Asia and South America, with North America being the only unrepresented region. The QCGC is heavily surgically-oriented and provides what is arguably the most extensive, comprehensive and intensive training in surgical oncology in Australia.

This report is the culmination of over a year's work in compiling and analysing prospectively collected data from patients' management, and would not have been possible but for the dedication and hard work of the gynaecological oncologists who work under its banner.

The QCGC has the largest and most detailed gynaecological cancer database of records in Australia, and quite possibly the world. Perusal of these reports shows survival curves out to 192 months, or 16 years. Mr Jackson collated the data and edited this report, Mr Tripcony performed detailed statistical analyses, and Dr Kondalsamy-Chennakesavan helped in interpreting and discussing the findings. I can't remember seeing such figures from anywhere else in the world.

This of course provides invaluable information not only on standard five-year survival and median survival but also on long term survival.

The database software used, the clinical administration system or CAS from Mirrabooka Systems Pty Ltd (http://www. mirrabooka.com/cas.shtml) has provided the means to accumulate this extensive and detailed collection of data.

A number of interesting and pleasing findings have come out of this analysis, and I would like to address a couple of these cases.

For each site we have compared the outcomes for two nine-year periods, 1984-1993 and 1994-2003. It is pleasing to see that for ovarian and uterine cancer the outcome in terms of survival has improved significantly with time. The analysis of ovarian cancer showed some very interesting results. The amount of residual disease left at the end of cytoreductive surgery was a very powerful determinant of survival, second only to disease stage. The results presented here are in respect to all stages of ovarian cancer.

It was realised that nil residuum would do extremely well because it would contain all of the stage I and stage II cases. However, this has also been shown to be the case for stage IIIC ovarian cancer; it seems that with stage IIIC of the disease, unless residual disease is reduced to less than one centimetre, there is little beneficial effect on survival.

These figures are not presented here as they will be the subject of a separate scientific publication, however, it does suggest that to date we have been too conservative in our approach to ovarian cancer surgery.

While we have been good at debulking surgery, we need to move to cytoreductive surgery, if necessary employing peritonectomy type operations in selected patients. The figures will otherwise be left to speak for themselves.

Audo

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Figure 1: Queensland Centre for Gynaecological Cancer total workload 1982-2006





Figure 3: Cervical cancer incidence 1982-2006



Figure 4: Uterine cancer incidence 1982-2006



Figure 5: Ovarian cancer incidence 1982-2006



Figure 6: Vulval cancer incidence 1982-2006



Figure 7: Vaginal cancer incidence 1982-2006



Figure 8: Fallopian tube cancer incidence 1982-2006



Procedures 1996-2006

Figure 9: Hysterectomy



Figure 10: Salpingo-oophorectomy



Procedures 1996-2006

Figure 11: Lymphadenectomy



Figure 12: Vaginal surgery



Procedures 1996-2006

Figure 13: Gastrointestinal surgery



Incidence and procedures results

Interpretation of results

The preceding section (pages 4-7) shows trends in QCGC's workload and the incidence data on all major gynaecological malignancies between 1982 and 2006. Figure 1 shows a gradual increase in the numbers of patients treated at QCGC from 1982 to 1995. The increase in workload is more dramatic between 2002 and 2006. Such an increase in workload could possibly be because of the improved survival of patients treated for gynaecological malignancies along with a steady increase in the incidence of gynaecological cancers during this period.

Figure 2 shows the incidence of gynaecological cancers from 1982 to 2006. We have presented incidence data from our QCGC database and compared it with the incidence data reported by the Queensland Cancer Registry (QCR). Both show a gradual increase in the incidence of gynaecological malignancies over this time period.

Figures 3 to 8 show the incidence data on all major gynaecological malignancies from 1982 to 2006. The incidence of all gynaecological malignancies shows an increasing trend with the exception of cervical cancer. Decrease in the incidence of cervical cancer can partially be attributed to successful screening and management programs.

Figures 9 to 13 show the numbers of surgical procedures performed at QCGC between 1996 and 2006. Hysterectomy and salpingooophorectomy were the most common major surgical procedures performed.

The rest of the report provides detailed statistics on outcomes of major gynaecological cancers.

Statistical analysis

Outcome statistics on mortality ultimately shape the treatment given to patients. They also serve as a comparison with other oncology centres and provide effective feedback to clinicians working in the field.

Survival analysis is concerned with measuring the risk of occurrence of an outcome event as a function of time. The duration of time is calculated from the date of diagnosis until the event occurs and uses the survival curve to describe its distribution. Therefore, the outcome variable of interest is time until an event occurs.

In this report, the end point for the survival curves is disease-specific death. Time is measured in months and is calculated by subtracting the date last seen from the date of diagnosis.

Median survival can be considered to be the expectation of life. When the probability of survival reaches 50%, the corresponding time value on the X-axis is the median survival time.

Relapse-free survival is calculated from the date of diagnosis to the time of first local/distant failure or date last seen if there is no event. If the patient dies due to the cancer and there is no recorded relapse date then the date of death is taken to be the date of relapse. Deaths are defined as an event if the patient died:

- 1. Due to cancer
- 2. Resulting from treatment
- 3. Unknown cause.

Survival data is censored for the following reasons:

- Withdrawals from study (patient lost to follow-up)
- 2. An intervening event (intercurrent death)
- 3. Discharged after at least a 10 year period.

The Kaplan-Meier survival curve estimate is obtained by multiplying together the proportions of survivors up to and including the given failure time. The curve remains horizontal between each failure time.

A 95% confidence interval is calculated and plotted for each group estimate; patients at risk and median survival are displayed under the graph.

Survival curves are calculated for specific time periods. In this report time periods of 60 months/five years, 120 months/10 years and 192 months/16 years are used depending on the length of follow-up. The numbers displayed on each curve represent the following information. Likewise, salvage survival is defined as the period of time from the date of recurrence to the date last seen or date of death. For example, A% (B-C)

- A= Percent survival
- B= Number in group at risk at the start
- C= Number in group remaining due to events and censoring.

An in-series patient means primary management at or by the QCGC. A non in-series patient refers to primary management carried out elsewhere and these have been excluded from the analysis.

A Cox proportional hazards model is applied to evaluate the independent significance of prognostic factors such as age, FIGO stage, histology, differentiation and presentation period. Univariate and multivariate tables are constructed for both relapse free and disease specific end points at the various gynaecological sites.

In the multivariate tables, hazard or relative risk is the ratio of events between groups. Therefore a hazard of 1.0 means no difference between groups.

Table 1: Patient characteristics

Presentation period 1984-2003 (N=2903)

		1984-1993	1994-2003	
Factor		N=1428 (%)	N=1475 (%)	p-value
FIGO stage	I	889 (62)	976 (66)	
	Ш	282 (20)	257 (17)	
	Ш	203 (14)	187 (13)	0.16
	IV	52 (4)	54 (4)	
	Unknown	2 (0)	1 (0)	
Morphology	SCC	1127 (79)	1085 (74)	
	AdenoCa	220 (15)	286 (19)	
	AdenoSq	80 (6)	99 (7)	0.004**
	Other	1 (0)	5 (o)	
Differentiation	Well	182 (13)	254 (17)	
	Moderate	629 (44)	583 (40)	
	Poor	377 (26)	374 (25)	0.003**
	Other/unknown	240 (17)	264 (18)	
Age (years)	< 30	86 (6)	101 (7)	
	30-39	329 (23)	359 (24)	
	40-49	314 (22)	364 (25)	
	50-59	215 (15)	236 (16)	0.02*
	60-69	245 (17)	195 (13)	
	70-79	169 (12)	143 (10)	
	80+	70 (5)	77 (5)	
Treatment modality	Sx alone	587 (41)	655 (44)	
	RT alone	366 (26)	282 (19)	
	C alone	4 (o)	4 (o)	
	Sx+RT	358 (25)	208 (14)	
	RT+C	30 (2)	162 (11)	
	Sx+C	9 (1)	7 (1)	<0.001**
	Sx+RT+C	60 (4)	134 (9)	
	Other	14 (1)	23 (2)	

Table 2: Kaplan and Meier disease specific survival (DSS) estimates and 95% confidence intervals

Presentation period 1984-2003.

E.g. (5/10/16) year (DSS) estimate x% [95% CI]

Period	1984-1993	1994-2003
5 year	71.9 [69.5,74.3]	75.8 [73.3,78.3]
10 year	70.0 [65.4,70.5]	72.6 [69.6,75.6]
16 year	66.3 [63.6,69.0]	n/a

FIGO stage	I	П	ш	IV
5 year	87.9 [86.3,89.5]	63.9 [59.4,68.5]	29.9 [24.6,35.2]	10.7 [4.4,17.1]
10 year	84.2 [82.2,86.2]	58.7 [53.7,63.7]	25.7 [20.2,31.1]	_
16 year	82.2 [79.8,84.7]	57.9 [52.7,63.0]	23.3 [17.5,29.2]	_

Morphology	SCC	AdenoCa	AdenoSq
5 year	73.5 [71.5,75.5]	81.1 [77.4,84.8]	54.7 [46.9,62.5]
10 year	70.0 [67.8,72.1]	75.4 [71.0,80.0]	52.2 [44.0,60.4]
16 year	68.2 [65.7,70.7]	73.3 [68.3,78.3]	-

Differentiation	Well	Moderate	Poor	Other
5 year	89.6 [86.5,92.6]	73.1 [70.5,75.8]	60.6 [56.8,64.4]	80.1 [76.2,83.9]
10 year	88.2 [84.9,91.6]	67.9 [64.8,70.9]	56.7 [52.7,60.8]	77.9 [73.7,82.1]
16 year	86.4 [82.3,90.5]	66.8 [63.5,70.0]	54.4 [49.5,59.2]	75.7 [70.9,80.4]

Age (years)	< 30	30-39	40-59	60+
5 year	77.3 [70.8,83.9]	81.6 [78.5,84.7]	76.2 [73.6,78.9]	63.2 [59.7,66.6]
10 year	-	79.3 [76.0,82.7]	72.2 [69.2,75.2]	57.3 [53.4,61.2]
16 year	-	78.9 [75.4,82.3]	70.4 [67.0,73.9]	53.9 [49.2,58.5]

Treatment	RT alone	Sx alone	Sx+RT	RT+C	Sx+RT+C
5 year	47.1[42.9,51.4]	95.1[93.8,96.4]	69.8[65.8,73.7]	47.7[38.4,57.1]	61.0[52.9,69.1]
10 year	41.8[37.2,46.4]	92.4[90.7,94.2]	64.2[59.8,68.5]	_	55.7[46.1,65.2]
16 year	37.1[31.6,42.6]	91.6[89.7,93.6]	62.4 [57.4,67.4]	-	55.7[46.1,65.2]

Table 3: Univariate Cox model

Presentation period 1984-2003.

			DSS			RFS	
Factor		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	П	3.16	[2.6,3.8]	0.0**	2.89	[2.42,3.45]	0.0**
	ш	8.97	[7.5,10.8]	0.0**	7.06	[6.0,8.4]	0.0**
	IV	21.98	[17.4,28.2]	0.0**	15.9	[12.5,20.3]	0.0**
Morphology							
SCC vs	AdenoCa	0.74	[0.6,0.9]	0.006**	0.79	[0.7,1.0]	0.02*
	AdenoSq	1.87	[1.5,2.4]	0.0**	1.86	[1.5,2.3]	0.0**
	Other	1.68	[0.2,12.0	0.6	1.19	[0.2,8.5]	0.86
Period							
1984-1993 vs	1994-2003	0.85	[.7,1.0]	0.03*	0.86	[0.8,1.0]	0.03*
Differentiation							
Well vs	Moderate	2.83	[2.1,3.9]	0.0**	2.47	[1.9,3.2]	0.0**
	Poor	4.53	[3.3,6.2]	0.0**	3.82	[2.9,5.0]	0.0**
	Other	1.97	[1.38,2.8]	<0.001 **	1.6	[1.2,2.2]	0.004**
Age							
40-59 years vs	<30	0.82	[0.6,1.2]	0.27	0.79	[0.6,1.1]	0.15
	30-39	0.72	[0.6,0.9]	0.002**	0.69	[0.6,0.8]	<0.001**
	60+	1.68	[1.4,2.0]	0.0**	1.55	[1.3,1.8]	<0.001**
Treatment							
RT vs	Sx	0.08	[0.06,0.1]	0.0**	0.11	[0.09,0.14]	0.0**
	RT+Sx	0.45	[0.38,0.5]	0.0**	0.51	[0.43,0.61]	0.0**
	RT+C	0.97	[0.7,1.3]	0.83	0.99	[0.78,1.26]	0.94
	Sx+RT+C	0.59	[0.45,0.78]	<0.001**	0.67	[0.52,0.85]	<0.001**
	Other	1.89	[1.34,2.66]	<0.001 **	1.73	[1.24,2.44]	<0.001**

Table 4: Multivariate Cox model

Presentation period 1984-2003.

			DSS			RFS	
Factor		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	II	1.58	[1.27,1.97]	<0.001 ^{**}	1.55	[1.26,1.9]	<0.001 ^{**}
	III	3.93	[3.11,4.97]	0.0**	3.41	[2.73,4.27]	<0.001 ^{**}
	IV	9.31	[6.99,12.4]	0.0**	6.89	[5.23,9.07]	<0.001 **
Morphology							
SCC vs	AdenoCa	1.24	[0.99,1.54]	0.06	1.24	[1.02,1.52]	0.03
	AdenoSq	1.59	[1.24,2.04]	<0.001 ^{**}	1.64	[1.29,2.08]	<0.001 ^{**}
	Other	4.46	[0.62,32.1]	0.14	2.99	[0.42,21.4]	0.28
Period							
1984-1993 vs	1994-2003	0.91	[0.78,1.06]	0.22	0.91	[0.79,1.05]	0.21
Differentiation							
Well vs	Moderate	1.62	[1.18,2.22]	0.003**	1.46	[1.11,1.93]	0.008**
	Poor	2.1	[1.52,2.89]	<0.001 ^{**}	1.8	[1.36,2.4]	<0.001 ^{**}
	Other	1.14	[0.79,1.63]	0.5	0.93	[0.67,1.29]	0.67
Age							
40-59 years vs	< 30	1.55	[1.09,2.2]	0.02*	1.3	[0.94,1.81]	0.12
	30-39	1.19	[0.96,1.48]	0.12	1.06	[0.86,1.29]	0.6
	60+	1.07	[0.89,1.28]	0.47	1.01	[0.86,1.2]	0.87
Treatment							
RT vs	Sx	0.19	[0.14,0.26]	0.0**	0.25	[0.19,0.34]	<0 . 001**
	RT+Sx	0.81	[0.65,1.01]	0.06	0.85	[0.69,1.05]	0.14
	RT+C	0.89	[0.68,1.17]	0.4	0.93	[0.72,1.2]	0.58
	Sx+RT+C	0.85	[0.63,1.13]	0.26	0.92	[0.7,1.21]	0.54
	Other	2.22	[1.54,3.21]	<0.001 ^{**}	2.17	[1.5,3.12]	<0.001 ^{**}



Figure 14: Overall survival 1984-2003 by FIGO stage

Figure 15: Relapse free survival 1984-2003 by FIGO stage



Figure 16: Overall survival 1984-2003 FIGO stage I by age



Figure 17: Overall survival 1984-2003 FIGO stage II-IV by age





Figure 18: Overall survival 1984-1993 by FIGO stage

Figure 19: Overall survival 1994-2003 by FIGO stage





Figure 20: Relapse free survival 1984-1993 by FIGO stage







Figure 22: Salvage survival 1984-2003 by site of relapse





Interpretation of results

Table 1 shows the key characteristics of all patients who were treated for cervical cancer at QCGC. We have grouped patients into two categories based on the year in which they presented (1984 to 1993 and 1994 to 2003). It is interesting to note that all the key characteristics (tumour morphology, differentiation and treatment modality) differed between these two groups, with the exception of FIGO staging.

Table 2 shows disease specific survival estimates (five, 10 and 16 years) and 95% confidence intervals, by key characteristics. The five-year survival rates achieved at QCGC is significantly better than the survival rates reported by FIGO in their latest report (Volume 26).

Tables 3 and 4 show univariate and multivariate Cox proportional hazards models respectively, evaluating the significance of prognostic factors such as age, FIGO stage, treatment time-period, morphology, grade and treatment modality. Univariate analyses (Table 3) showed significant decline in their risk if they presented between 1994 and 2003 when compared to the previous time-period (1984 to 1993). However, this statistical significance did not persist in our multivariate model (Table 4).

Figures 14 and 15 show overall and relapse-free survival between 1984 and 2003, by FIGO stages. Overall survival (95% Cl) and relapse-free survival (95% Cl) at 192 months was 68% (66-70%) and 65% (63-67%) respectively. Figures 16 and 17 show the influence of age categories (<50 years and > 50 years) on overall survival by FIGO stages. Figures 18 to 21 show overall and relapse-free survival at five years, by FIGO stage. These results achieved seem to be better than the results published by FIGO in their triennial report. Figure 22 shows the outcomes of salvage survival by site of relapse. Figure 23 shows the outcomes of salvage survival by treatment type for relapse. With the exception of few case reports and case series, published literature on salvage survival for cervical cancer is negligible and formal comparisons can not be made at this point in time.

Table 5: Patient characteristics

Presentation period 1984-2003 (N=2119)

		1984-1993	1984-1993	
Factor		N=834 (%)	N=1286 (%)	p-value
FIGO stage	L	221 (26)	406 (32)	
	Ш	95 (11)	113 (9)	0.59
	Ш	423 (51)	648 (50)	
	IV	3 (1)	5 (o)	
	Unknown			
Morphology	Ser/PapSer	337 (40)	526 (41)	
	AdenoCa	75 (9)	60 (5)	
	Endometriod	102 (12)	132 (10)	
	Mucinous	70 (8)	157 (12)	<0.001 **
	Mull+Meso	23 (3)	38 (3)	
	Clear cell	140 (17)	152 (12)	
	Other	20 (2)	7 (1)	
Differentiation	Well	91 (11)	129 (10)	
	Moderate	186 (22)	246 (19)	
	Poor	299 (36)	569 (44)	0.02*
	Other/unknown	258 (31)	342 (27)	
Age (years)	< 30	54 (6)	62 (5)	
	30-39	43 (5)	89 (7)	
	40-49	134 (16)	182 (14)	
	50-59	198 (24)	342 (27)	<0.001**
	60-69	238 (29)	289 (23)	
	70-79	137 (16)	246 (19)	
	80+	30 (4)	76 (6)	

		1984-1993	1984-1993	
Factor		N=834 (%)	N=1286 (%)	p-value
Treatment modality	Sx alone	149 (18)	297 (23)	
	RT alone	1 (0)	o (o)	
	C alone	11 (1)	9 (1)	
	Sx+RT	21 (3)	3 (0)	
	RT+C	1 (0)	o (o)	<0.001**
	Sx+C	611 (73)	958 (75)	
	Sx+RT+C	32 (4)	11 (11)	
	Other	8 (1)	8 (1)	

Table 6: Kaplan and Meier disease specific survival (DSS) estimates and 95% confidence intervals

Presentation period 1984-2003.

E.g. (5/10/16) year (DSS) estimate x% [95% CI].

Period	1984-1993	1994-2003
5 year	46.9[43.4,50.4]	53.4[50.1,56.8]
10 year	37.9[34.4,41.3]	39.7[33.6,45.8]
16 year	34.8[31.2,38.4]	_

FIGO stage	I	П	Ш	IV
5 year	88.9[86.2,91.6]	65.1[57.8,72.4]	32.6[29.3,35.9]	12.4[6.8,17.9]
10 year	82.9[79.2,86.6]	53.2[44.4,62.0]	18.4[15.1,21.7]	5.5[0,10.4]
16 year	81.1[76.9,85.3]	49.0[39.1,58.9]	15.1[11.5,18.6]	n/a

Morphology	Ser/PapSer	AdenoCa	Endometrioid	Mucinous
5 year	37.5[33.9,41.1]	29.8[20.8,38.8]	66.7[59.9,73.5]	74.8[68.7,80.8]
10 year	25.5[21.7,29.3]	17.7[8.9,26.5]	57.2[49.4,65.0]	68.6[61.0,76.3]
16 year	22.2[18.1,26.4]	14.7[5.6,23.8]	55.2[46.8,63.7]	-

Morphology	Mull+Meso	Clear cell	Other
5 year	27.4[14.9,39.8]	59.9[52.1,67.6]	69.7[64.3,75.2]
10 year	10.1[0.0,21.2]	50.6[41.7,59.6]	61.0[54.1,67.5]
16 year	-	46.2[36.2,56.3]	56.4[48.5,64.4]

Differentiation	Well	Moderate	Poor	Other
5 year	86.7[81.9,91.5]	51.7[46.5,57.0]	35.8[32.0,39.6]	57.4[53.1,61.8]
10 year	79.8[73.1,86.5]	40.5[34.6,46.4]	21.3[17.2,25.5]	49.8[45.0,54.6]
16 year	68.3[57.8,78.9]	36.9[30.3,43.6]	19.7[15.3,24.1]	48.7[43.7,53.6]

Age (years)	40	40-59	60+
5 year	77.0[71.3,82.6]	53.7[50.0,57.5]	42.1[38.5,45.6]
10 year	74.1[67.8,80.4]	43.8[39.7,47.9]	28.5[24.5,32.4]
16 year	71.4[64.4,78.5]	40.3[35.7,45.0]	25.0[20.3,29.7]

Treatment	Sx alone	Sx+C	Sx+RT+C
5 year	78.8[74.7,83.0]	45.3[42.5,48.1]	33.6[19.3,48.0]
10 year	74.0[68.7,79.0]	34.3[31.2,37.3]	15.2[3.8,26.5]
16 year	-	30.4[27.0,33.9]	11.4[1.0,22.1]

Table 7: Univariate Cox model

Presentation period 1984-2003.

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	П	3.42	[2.5,4.69]	<0.001**	4.0	[3.04,5.26]	<0.001**
	Ш	8.8	[6.99,11.1]	<0.001**	9.42	[7.65,11.6]	<0.001**
	IV	17.94	[13.7,23.5]	<0.001 **	14.6	[11.4,18.7]	<0.001 **
Morphology							
Ser/PapSer vs	AdenoCa	1.43	[1.14,1.79]	<0.001 **	1.25	[1.01,1.54]	0.04*
	Endometroid	0.44	[0.34,0.56]	<0.001**	0.42	[0.34,0.51]	<0 . 001**
	Mucinous	0.34	[0.26,0.45]	<0.001**	0.28	[0.21,0.36]	<0.001**
	Mull+Meso	1.83	[1.35,2.48]	<0.001**	1.53	[1.15,2.03]	0.003**
	Clear cell	0.59	[0.47,0.76]	<0.001 ^{**}	0.49	[0.39,0.62]	<0.001 **
Period							
1984-1993 vs	1994-2003	0.78	[0.68,0.88]	<0.001**	0.81	[0.72,0.91]	<0.001 ^{**}
Differentiation							
Well vs	Moderate	3.64	[2.6,5.1]	<0.001**	3.22	[2.4,4.3]	<0.001 **
	Poor	5.33	[3.86,7.35]	<0.001**	4.76	[3.6,6.3]	<0.001 ^{**}
	Other	3.06	[2.2,4.27]	<0.001**	2.57	[1.9,3.4]	<0.001**
Age							
40-59 years vs	∢ 40 years	0.43	[0.32,0.56]	<0.001 ^{**}	0.44	[0.35,0.57]	<0.001**
	6o+years	1.47	[1.29,1.67]	<0.001**	1.37	[1.22,1.54]	<0.001**
Treatment							
Sx vs	Sx+C	2.88	[2.32,3.58]	<0.001 **	3.42	[2.79,4.2]	<0.001**
	Sx+RT+C	4.27	[2.9,6.3]	<0.001**	4.54	[3.12,6.54]	<0.001 ^{**}

Table 8: Multivariate Cox model

Presentation period 1984-2003.

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	П	4.35	[3.07,6.17]	<0.001 **	4.26	[3.14,5.78]	<0.001 ^{**}
	Ш	11.58	[8.64,15.5]	<0.001**	9.65	[7.44,12.5]	<0.001 **
	IV	21.4	[15.3,29.7]	<0.001**	13.82	[10.2,18.6]	<0.001 **
Morphology							
Ser/PapSer vs	AdenoCa	1.08	[0.86,1.37]	<0.001**	1.02	[0.82,1.26]	0.87
	Endometrioid	0.8	[0.62,1.02]	0.07	0.72	[0.58,0.9]	0.003*
	Mucinous	1.41	[1.05,1.89]	0.02*	1.1	[0.83,1.44]	0.5
	Mul+Mes	1.76	[1.3,2.4]	<0.001**	1.59	[1.19,2.12]	<0.001**
	Clear cell	1.59	[1.23,2.05]	<0.001**	1.26	[0.99,1.61]	0.06
Period							
1984-1993 vs	1994-2003	0.74	[0.65,0.85]	<0.001**	0.8	[0.71,0.91]	<0.001 **
Differentiation							
Well vs	Moderate	2.46	[1.75,3.47]	<0.001**	2.03	[1.51,2.73]	<0.001**
	Poor	2.73	[1.95,3.81]	<0.001**	2.2	[1.65,2.93]	<0.001**
	Other	2.61	[1.86,3.66]	<0.001**	1.99	[1.48,2.67]	<0.001**
Age							
40-59 years vs	<40 years	0.74	[0.55,0.98]	0.04*	0.73	[0.57,0.95]	0.02*
	60+years	1.34	[1.17,1.53]	<0.001**	1.24	[1.1,1.4]	<0.001**
Treatment							
Sx vs	Sx+C	0.51	[0.39,0.66]	0.006**	0.68	[0.54,0.87]	<0 . 001**
	Sx+RT+C	0.56	[0.37,0.85]	<0.001 **	0.70	[0.47,1.05]	0.09



Figure 24: Overall survival 1984-2003 by FIGO stage







Figure 26: Overall survival 1984-2003 by presentation period







Figure 28: Overall survival 1984-1993 by FIGO stage







Figure 30: Relapse free survival 1984-1993 by FIGO stage

Figure 31: Relapse free survival 1994-2003 by FIGO stage





Figure 32: Salvage survival 1984-2003 by site of relapse





Interpretation of results

Table 5 shows the key characteristics of patients diagnosed with ovarian cancer by presentation period. With the exception of FIGO staging, all the key characteristics (age, morphology, grade and treatment modality) differed significantly between these two time periods.

Table 6 shows disease specific survival estimates (five, 10 and 16 years) and 95% confidence intervals, by key characteristics. The fiveyear survival rate achieved at QCGC for malignant ovarian tumours is better than the survival rates reported by FIGO in their latest report (volume 26).

Tables 7 and 8 show univariate and multivariate Cox proportional hazards models respectively, evaluating the significance of prognostic factors such as age, FIGO stage, treatment time-period, morphology, grade and treatment modality. Univariate analyses (Table 7) showed significant decline in their risk if they presented between the years 1994-2003 when compared to the previous time-period (1984 to 1993). This statistical significance persisted in our multivariate model (Table 4) after adjusting for other key prognostic factors. It is possible that availability of better chemotherapeutic regimens and newer drugs in the recent presentation period could have resulted in significant improvements when compared to the previous presentation period.

Figures 24 and 25 show overall and relapse-free survival between 1984 and 2003, by FIGO stages. Overall survival (95% CI) and relapse-free survival (95% CI) at 16 years was 37% (34-40%) and 34% (31-36%) respectively. Figures 26 and 27 show overall and relapse-free survival at five years by presentation period. These survival curves show significant improvement in the recent presentation period compared to the previous presentation period. Figure 28 shows 47% overall survival at five years for the time period 1984 to 1993. Overall survival at five years was 53% for the time period 1994 to 2003 (Figure 29). Between 1984 and 1993, the relapse-free survival rate was 35% at five years (Figure 30). In the recent time period (1994 to 2003), the relapse-free survival at five years has improved to 42% (Figure 31). Figures 32 and 33 show five-year salvage survival curves for ovarian cancer. Between 1982 and 2003, the overall salvage survival (95% CI) at five years was 13% (10-15%). There is a paucity of information on salvage survival for ovarian cancer in the published literature and no reasonable comparisons can be made.

Fallopian tube cancer

Table 9: Patient characteristics

Presentation period 1984-2003 (N=52)

		1984-1993	1994-2003	
Factor		N=18 (%)	N=34 (%)	p-value
FIGO stage	I	8 (44)	11 (32)	
	П	3 (17)	11 (32)	0.56
	Ш	7 (39)	12 (35)	
	IV	o (o)	o (o)	
	Unknown	o (o)	o (o)	
Morphology	AdenoCa	7 (39)	5 (15)	
	PapSer	4 (22)	15 (44)	0.1
	Other	7 (39)	14 (41)	
Differentiation	Well	o (o)	o (o)	
	Moderate	6 (33)	7 (21)	0.02*
	Poor	5 (28)	23 (68)	
	Other/unknown	7 (39)	4 (12)	
Age (years)	< 30	o (o)	o (o)	
	30-39	o (o)	2 (6)	
	40-49	4 (22)	7 (21)	0.75
	50-59	6 (33)	9 (26)	
	60-69	5 (28)	7 (21)	
	70-79	2 (11)	8 (23)	
	80+	1 (1)	1 (3)	
Treatment modality	Sx alone	2 (11)	3 (9)	
	RT alone	o (o)	o (o)	
	C alone	o (o)	o (o)	
	Sx+RT	1 (6)	o (o)	0.13
	RT+C	o (o)	o (o)	
	Sx+C	11 (61)	29 (85)	
	Sx+RT+C	4 (22)	2 (6)	
	Other	o (o)	o (o)	
Table 10: Kaplan and Meier disease specific survival (DSS) estimates and 95% confidence intervals

68.1 [48.6,87.5]

Presentation period 1984-2003.

5 year

E.g. Five year (DSS) estimate x% [95% CI].

Period			1984-19	93			1994-2003		
5 year			71.1 [49.7,92.5]			63.7 [37.3,90.0]			
	_								
FIGO stage	1			П		111			IV
5 year	68.0	68.0 [44.7,91.3]		78.6 [51.3,10	o]	72.0 [48	.1,95.8]		n/a
Morphology AdenoCa		AdenoCa	PapSer		Other		Other	r	
5 year		65.5 [32.8,	98.1] 54.3 [19.,89.6		6] 79.5 [79.5 [58.3,100]	
	1								
Differentiation	Well			Moderate		Poor			Other
5 year	N/A			80.7 [56.1,10	66.3 [41.2,91.5]			62.3 [32.9,91.7]	
Age (years)			< 50				>=50		
5 year 74.1 [42			74.1 [42.	.1 [42.5,100]		67.6 [49.4,85.9]			
Treatment			Sx+C				Sx+RT+C		

50 [10.0,90.0]

Table 11: Univariate Cox model

Presentation period 1984-2003.

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	Ш	1.89	[0.51,7.09]	0.34	2.25	[0.72,7.02]	0.16
	III	1.96	[0.59,6.52]	0.27	4.21	[1.58,11.2]	0.004**
Morphology							
AdenoCa vs	PapSer	1.07	[0.28,4.05]	0.92	1.49	[0.52,4.3]	0.46
	Other	0.82	[0.23,2.92]	0.76	0.99	[0.34,2.91]	0.99
Period							
1984-1993 vs	1994-2003	0.85	[0.28,2.61]	0.77	0.81	[0.37,1.76]	0.59
Differentiation							
Well vs	Moderate	0.34	[0.07,1.7]	0.19	0.34	[0.09,1.3]	0.11
	Poor	0.89	[0.29,2.71]	0.83	1.3	[0.53,3.23]	0.57
Age							
<50 years vs	50+	2.5	[0.56,11.1]	0.23	2.97	[0.89,9.89]	0.08
Treatment							
Sx+C vs	Sx+C+RT	1.97	[0.66,5.86]	0.23	1.07	[0.4,2.86]	0.9

Table 12: Multivariate Cox model

Presentation period 1984-2003.

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	П	1.73	[0.38,7.89]	0.48	1.57	[0.47,5.28]	0.46
	III	1.52	[0.39,5.9]	0.54	3.05	[1.03,9.05]	0.04*
Morphology							
AdenoCa vs	PapSer	0.7	[0.11,4.33]	0.7	0.94	[0.25,3.57]	0.93
	Other	0.15	[0.01,1.84]	0.14	0.62	[0.13,2.97]	0.55
Period							
1984-1993 vs	1994-2003	1.49	[0.25,8.99]	0.67	0.99	[0.3,3.31]	0.99
Differentiation							
Well vs	Moderate	0.53	[0.09,3.18]	0.49	0.54	[0.11,2.65]	0.45
	Poor	1.37	[0.27,6.85]	0.7	1.75	[0.45,6.76]	0.42
Age							
<50 years vs	50+	1.55	[0.28,8.47]	0.62	2.31	[0.63,8.5]	0.2
Treatment							
Sx+C vs	Sx+C+RT	11.2	[0.86,145.]	0.07	2.75	[0.47,16.1]	0.26



Figure 34: Overall survival 1984-2003 by FIGO stage







Figure 36: Overall survival 1984-2003 by presentation period

Figure 37: Relapse free survival 1984-2003 by presentation period





Figure 38: Overall survival 1984-1993 by FIGO stage

Figure 39: Overall survival 1994-2003 by FIGO stage





Figure 40: Relapse free survival 1984-1993 by FIGO stage







Figure 42: Salvage survival 1984-2003 by type of relapse





Interpretation of results

Table 9 shows key characteristics of patients diagnosed with fallopian tube cancer by presentation period. Eighteen patients were diagnosed with fallopian tube cancer between 1984 and 1993, and 34 were diagnosed with fallopian tube cancer between 1994 and 2003. All the key characteristics were similar between these time periods with the exception of tumour grades where the differences were statistically significant. Table 10 shows five-year disease specific survival estimates and 95% confidence intervals. Overall five-year survivals (95% CI) for the presentation periods 1984-1993 and 1994-2003 were 71% (50-92) and 64% (37-90) respectively. These differences were not statistically significant. However, these survival rates are better than the reported survival rates from FIGO.

Tables 11 and 12 show univariate and multivariate Cox proportional hazards models respectively, evaluating the significance of prognostic factors such as age, FIGO stage, treatment time-period, morphology, grade and treatment modality.

Figures 34 and 35 show overall and relapse-free survival between 1984 and 2003, by FIGO stages. Overall survival (95% CI) and relapse-free survival (95% CI) at 16 years was 46% (24-68%) and 36% (18-53%) respectively. Figures 36 and 37 show overall and relapse-free survival at five years by presentation period. No statistically significant differences in these survivals can be noticed between the presentation periods. Figures 38 to 41 show overall and relapse-free survival at five years by presentation periods and FIGO stages. Figures 42 and 43 show five-year salvage survival curves. Between 1982 and 2003, the overall salvage survival (95% CI) at five years was 23% (o-48%).

Table 13: Patient characteristics

Presentation period 1984-2003 (N=3380)

		1984-1993	1994-2003	
Factor		N=1266 (%)	N=2114 (%)	p-value
FIGO stage	I.	998 (79)	1518 (72)	
	П	85 (7)	178 (8)	<0.001**
	III	115 (9)	284 (13)	
	IV	63 (5)	118 (6)	
	Unknown	5 (o)	16 (1)	
Morphology#	Α	1087 (86)	1740 (82)	
	В	58(5)	140 (7)	
	С	42 (3)	93 (4)	0.05*
	D	32 (2)	56 (3)	
	Other	47(4)	85(4)	
Differentiation	Well	302 (24)	689 (33)	
	Moderate	307 (24)	739 (35)	
	Poor	152 (12)	404 (19)	0.43
	Other/unknown	505 (40)	282 (13)	
Age (years)	< 30	5 (o)	9 (0)	
	30-39	18 (1)	42 (2)	
	40-49	124 (10)	200 (9)	
	50-59	299 (24)	550 (26)	<0.001**
	60-69	427 (34)	609 (29)	
	70-79	320 (25)	504 (24)	
	80+	73 (6)	200 (9)	

			1984-1993	1994-2003	
Factor			N=1266 (%)	N=2114 (%)	p-value
Treatme	ent modality	Sx alone	210 (17)	1172 (55)	
		RT alone	15 (1)	34 (2)	
		C alone	4 (o)	3 (o)	
		Sx+RT	950 (75)	718 (34)	
		RT+C	2 (0)	4 (o)	<0.001 ^{**}
		Sx+C	24 (2)	82 (4)	
		Sx+RT+C	43 (3)	72 (3)	
		Other	18 (2)	29 (1)	
# Morph	ology				
А	AdenoCa				
	Papillary				
	AdenoSq				
	Endometrioid				
В	Mull				

Meso

CS

C PapSer

D LMS

Table 14: Kaplan and Meier disease specific survival (DSS) estimates and 95% confidence intervals

E.g. (5/10/16) year (DSS) estimate x% [95% CI].

Period		1984-19	93 1		1994-2003	994-2003		
5 year		80.5 [78	.3,82.7]		84.3 [82.5,86.1]	84.3 [82.5,86.1]		
10 year		77.7 [75.	3,80.1]		82.4 [80.3,84.6]			
16 year		77.2 [74	7,79.6]		n/a			
						1		
FIGO stage	1		П	Ш		IV		
5 year	92.8 [91.7,93.9		82.3 [76.9,87.8]	46.4 [40	5,52.3	10.6 [5.,16.2]		
10 year	90.3 [88.9,91.8]		78.8 [72.5,85.]	41.9 [35.	3,48.5]	7. [2.1,12.]		
16 year	1		73.7 [64.7,82.7]	41.9 [35.	3,48.5]	3. [0.,9.0]		
						1		
Morphology#	Α		В	C		D		
5 year	88.0 [86.6,89.3]		58.9 [50.9,66.8]	38.1 [27.	4,48.8]	40.5 [28.,53.1]		
10 year	85.6 [84.1,87.2]		51.7 [42.,61.4]	30.6 [19.	,42.1]	34.0 [20.6,47.4]		
16 year	85.1 [83.4,86.8]		_	26.8 [14.	5,39.1]	-		
Differentiation	Well		Moderate	Poor		Other		
5 year	97.4 [96.3,98.5]		87.9 [85.6,90.2]	54.3 [49.	5,59.1]	76.8 [73.7,80.]		
10 year	95.7 [94.1,97.4]		83.8[80.7,86.9]	52.1 [47.,	57.3]	74.1 [70.8,77.4]		
16 year	_		83.3 [80.1,86.5]	47.2 [39.	1,55.2]	-		
Age (years)			<50		>=50			
5 year			89.3 [86.,92.7]		81.8 [80.2,8	3.3]		
10 year			88.0 [84.2,91.6]		78.8 [77.1,80	0.6]		
16 year			87.9 [84.2,91.6]		78.1 [76.2,8	0.1]		

Treatment	RT alone	Sx alone	Sx+RT	Sx+C	Sx+RT+C
5 year	45.0 [25.3,64.8]	86.3 [84.2,88.4]	87. [85.2,88.7]	43.9 [33.1,54.7]	47-5 [37-,57-9]
10 year	_	83.7 [80.9,86.6]	84.2 [82.3,86.2]	37.6 [23.,52.3]	41.2[30.4,52.]
16 year	-	_	83.7 [81.6,85.8]	_	38.0 [26.4,49.6]

Table 15: Univariate Cox model

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	II	2.5	[1.81,3.57]	<0.001**	2.77	[2.1,3.66]	<0.001**
	ш	9.59	[7.7,11.84]	<0.001**	7.78	[6.45,9.4]	<0.001**
	IV	34.8	[27.6,43.7]	<0.001**	24.4	19.8,30.2]	<0.001**
Morphology#							
Morphology#	D			(0.004**			(0.004**
A VS	D	4.07	[3.0,0.0]	(0.001	4.49	[3.5/,5.05]	(0.001
		6.49	[5.0,8.5]	(0.001	5.05	[4.58,7.40]	(0.001
	U	2.99	[2.1,4.2]	(0.001	0.24	[4.08,8.3]	(0.001
Period							
1984-1993 vs	1994-2003	0.79	[0.7,0.9]	0.007**	0.87	[0.75,1.02]	0.08
Differentiation							
Well vs	Moderate	3.96	[2.7,5.9]	<0.001 **	2.77	[2.04,3.75]	<0.001 **
	Poor	18.0	[12.4,26.2]	<0.001 **	10.5	[7.87,14.1]	<0.001 ^{**}
	Other	7.8	[5.3,11.3]]	<0.001 **	5.0	[3.7,6.7]	<0.001 **
A							
Age		0	[]	. 44		, , ,	
<50 years vs	>=50 years	1.78	[1.29,2.46]	<0.001**	1.6	[1.2,2.1]	<0.001**
Treatment							
Sx vs	RT	4.25	[2.6,6.9]	<0.001**	3.74	[2.36,5.93]	<0.001 ^{**}
	RT+Sx	0.9	[0.7,1.1]	0.33	0.92	0.77,1.11]	0.38
	RT+C	5.7	[4.2,7.9]	<0.001 ^{**}	5.64	[4.25,7.5]	<0.001 ^{**}
	Sx+RT+C	4.3	[3.2,5.9]	<0.001**	4.08	[3.08,5.4]	<0.001**

Table 16: Multivariate Cox model

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	II	2.34	[1.6,3.3]]	<0.001**	2.62	[1.98,3.48]	<0.001**
	III	7.97	[6.36,9.99]	<0.001**	6.38	[5.2,7.8]	<0.001**
	IV	19.05	[14.5,25.0]	<0.001 ^{**}	12.7	[9.8,16.3]	<0.001 ^{**}
Morphology#							
A vs	В	2.37	[1.8,3.2]	<0.001**	2.18	[1.68,2.82]	<0.001**
	С	1.61	[1.18,3.2]	<0.001 **	1.51	[1.13,2.01]	<0.001**
	D	3.59	[2.48,5.2]	<0.001**	3.7	[2.6,5.2]	<0.001**
Period							
1984-1993 vs	1994-2003	0.54	[0.45,0.66]	<0 . 001**	0.61	[0.51,0.72]	<0 . 001**
Differentiation							
Well vs	Moderate	2.66	[1.79,3.95]	<0.001**	1.88	[1.38,2.57]	<0.001 ^{**}
	Poor	6.8	[4.6,10.1]	<0.001**	3.8	[2.8,5.2]	<0.001**
	Other	4.19	[2.8,6.2]	<0 . 001**	2.8	[2.1,3.8]	<0.001**
Age							
<50 years vs	>=50 years	2.65	[1.86,3.76]	<0.001 ^{**}	2.1	[1.55,2.84]	<0.001 ^{**}
Treatment							
Sx vs	RT	2.23	[1.35,3.68]	0.002**	1.95	[1.22,3.12]	0.005**
	RT+Sx	0.65	[0.52,0.8]	<0.001 ^{**}	0.7	[0.57,0.85]	<0.001**
	RT+C	0.58	[0.41,0.82]	<0.002 ^{**}	0.81	[0.59,1.12]	0.2
	Sx+RT+C	0.56	[0.4,0.79]	<0.001**	0.77	[0.56,1.06]	0.11

Figure 44: Overall survival 1984-2003 by FIGO stage



Figure 45: Relapse free survival 1984-2003 by FIGO stage





Figure 46: Overall survival 1984-2003 by presentation period

Figure 47: Relapse free survival 1984-2003 by presentation period





Figure 48: Overall survival 1984-1993 by FIGO stage

Figure 49: Overall survival 1994-2003 by FIGO stage



87% (998-777) S1 77% (1266-868) All 74% (85-52) S2 % relapse free 32% (115-32) S3 10% (63-5) S4 Months 95% CI Median All 75, 79] 85, 88] [S1 [S2 [65, 83] S3 20 months [23, 41] S4 [2, 17] 6 months

Figure 50: Relapse free 1984-1993 by FIGO stage







Figure 52: Salvage survival 1984-2003 by site of relapse





Interpretation of results

Table 13 shows the key characteristics of all those patients who were treated for uterine cancer at QCGC. We have grouped patients into two categories based on the year in which they presented (1984 to 1993 and 1994 to 2003). It is interesting to note that all the key characteristics (FIGO staging, tumour morphology, and treatment modality) differed between these two groups, with the exception of tumour grade/differentiation.

Table 14 shows disease specific survival estimates (five, 10 and 16 years) and 95% confidence intervals, by key characteristics. The fiveyear survival rate achieved at QCGC for uterine cancer is better than the survival rates reported by FIGO in their latest report (table 10, corpus uteri, volume 26). Tables 15 and 16 show univariate and multivariate Cox proportional hazards models respectively, evaluating the significance of prognostic factors such as age, FIGO stage, treatment time-period, morphology, grade and treatment modality. For disease specific survival in our multivariate model, it is interesting and important to note that those who presented in the recent time period (1994 to 2003) had a hazard ratio (95% CI) of 0.54 (0.45-0.66) when compared those presenting in 1984 to 1993. Similar pattern could be noticed for relapse-free survival with a hazard ratio (95% CI) of 0.61 (0.51-0.72).

Figures 44 and 45 show overall and relapse-free survival between 1984 and 2003, by FIGO stages. Overall survival (95% CI) and relapse-free survival (95% CI) at 192 months/16 years were 79% (78-81%) and 75% (73-77%) respectively. Figures 46 and 47 show overall and relapse-free survival at five years by presentation period. The overall survival curves show significant improvement in the recent presentation period compared to the previous presentation period. Detailed survival curves on overall and relapse-free survival by FIGO stages and presentation period are given in Figures 48-51. Data on salvage survivals for uterine cancer are provided in Figures 52 and 53, by site of relapse and by treatment modality, respectively.

Table 17: Patient characteristics

Presentation period 1984-2003 (N=216)

		1984-1993	1994-2003	
Factor		N=68 (%)	N=80 (%)	p-value
FIGO stage	I.	25 (36)	12 (31)	
	II	17 (25)	27 (34)	
	III	16 (24)	13 (16)	0.53
	IV	10 (15)	11 (14)	
	Unknown	0	4 (5)	
Morphology	SCC	58 (85)	60 (75)	
	AdenoCa	5 (7)	6 (7)	0.18
	Other	5 (7)	14 (18)	
Differentiation	Well	5 (7)	6 (7)	
	Moderate	15 (22)	23 (29)	<0.001**
	Poor	11 (16)	33 (41)	
	Other/unknown	37 (54)	18 (23)	
Age (years)	< 30	2 (3)	1 (0)	
	30-39	4 (6)	4 (5)	
	40-49	5 (7)	10 (13)	
	50-59	10 (15)	15 (19)	0.43
	60-69	16 (24)	18 (23)	
	70-79	22 (32)	15 (19)	
	80+	9 (13)	17 (21)	
Treatment modality	Sx alone	8 (12)	12 (15)	
	RT alone	37 (54)	30 (38)	
	C alone	o (o)	o (o)	
	Sx+RT	14 (21)	13 (16)	
	RT+C	5 (7)	14 (18)	0.11
	Sx+C	o (o)	o (o)	
	Sx+RT+C	1 (1)	6 (8)	
	Other	3 (4)	5 (6)	

Table 18: Kaplan and Meier disease specific survival (DSS) estimates and 95% confidence intervals

Presentation period 1984-2003.

E.g. Five year (DSS) estimate x% [95% CI].

Period			1984-1993			1994-2003				
5 year			53.0 [40.9,65.1]			52.6 [39.2,66.0]				
FIGO Stage	I			П		III			IV	
5 year	75.4 [62.6,88.2]		58.7 [42.0,75	.3]	27.7 [9.0	27.7 [9.0,46.5]		22.9 [4.4,41.3]	
Morphology	Morphology SCC				AdenoCa			Other	r	
5 year	54.8 [45.1,64		,64.5]	24.9 [0.0,54.2]		2]	61.8 [36.8,86.7]	
Differentiation	Well			Moderate		Poor			Other	
5 year	90.9	73.9,100]		60.7 [43.4,77	.9]	44.0 [28	.0,60.1]		47.4 [32.5,62.2]	
Age (years)	< 40			40-59		60-69			70+	
5 year	66.3	34.4,98.2]		57.6 [40.7,74.	5]	56.0 [38	.5,73.4]		46.2 [32.2,60.3]	
Treatment	RT alo	one		Sx alone		Sx+RT			RT+C	
5 year	41.0 [28.4,53.7]		81.3 [62.1,10	o]	64.0 [44	.9,83.0]		49.5 [21.3,77.6]	

Table 19: Univariate Cox model

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	П	1.65	[0.79,3.4]	0.18	1.44	[0.74,2.8]	0.28
	ш	4.01	[1.96,8.18]	<0.001**	2.79	[1.43,5.4]	0.003**
	IV	6.17	[2.9,12.9]	<0.001**	4.2	[2.13,8.4]	<0.001**
Morphology							
SCC vs	AdenoCa	1.55	[0.7,3.4]	0.28	1.26	[0.57,2.76]	0.57
	Other	0.85	[0.37,2.0]	0.71	0.86	[0.39,1.9]	0.7
Period							
1984-1993 vs	1994-2003	0.93	[0.56,1.53]	0.77	0.84	[0.53,1.35]	0.47
Differentiation							
Well vs	Moderate	5.2	[0.69,38.9]	0.11	2.8	[0.66,12.0]	0.16
	Poor	8.7	[1.2,63.6]	0.03*	4.5	[1.09,18.6]	0.04*
	Other	7.6	1.04,54.9]	0.05*	4.77	[1.17,19.5]	0.03*
Age							
<40 years vs	40-59	1.36	[0.4,4.7]	0.62	1.52	[0.45,5.2]	0.5
	60-69	1.4	[0.4,4.9]	0.58	1.94	[0.57,6.57]	0.28
	70+	2.05	[0.63,6.72]	0.23	2.34	[0.7,7.6]	0.16
Treatment							
RT vs	Sx	0.28	[0.1,0.78]	0.02*	0.54	[0.24,1.2]	0.13
	RT+Sx	0.5	[0.24,1.03]	0.06	0.63	[0.3,1.23]	0.17
	RT+C	0.72	[0.34,1.55]	0.4	0.8	[0.39,1.7]	0.59

Table 20: Multivariate Cox model

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	н	1.31	[0.6,2.87]	0.49	1.22	[0.6,2.48]	0.57
	ш	3.79	[1.66,8.65]	0.002**	2.73	[1.27,5.8]	0.01**
	IV	5.14	[2.4,11.0]	<0.001 ^{**}	3.83	[1.87,7.8]	<0.001 **
Morphology							
SCC vs	AdenoCa	2.3	[0.9,5.6]	0.07	1.5	[0.64,3.5]	0.35
	Other	0.75	[0.26,2.1]	0.58	0.61	[0.22,1.7]	0.34
Period							
1984-1993 vs	1994-2003	1.00	[0.51,1.96]	0.99	0.96	[0.51,1.8]	0.89
Differentiation	1						
Well vs	Moderate	3.46	[0.45,26.8]	0.23	5.55	[1.26,24.5]	0.02
	Poor	6.3	[0.8,49.8]	0.08	3.2	[0.72,14.3]	0.13
	Other	6.47	[0.8,49.7]	0.07	3.88	[0.89,16.9]	0.07
Age							
∢40 years vs	40-59	0.89	[0.23,3.37]	0.86	1.18	[0.32,4.3]	0.8
	60-69	1.00	[0.27,3.67]	1.0	1.76	[0.49,6.3]	0.38
	70+	0.95	0.25,3.57]	0.94	1.6	[0.44,5.9]	0.48
Treatment							
RT vs	Sx	0.4	[0.12,1.33]	0.14	0.89	[0.34,2.34]	0.81
	RT+Sx	0.54	[0.22,1.29]	0.16	0.81	[0.36,1.79]	0.6
	RT+C	0.65	[0.26,1.6]	0.35	0.96	[0.41,2.24]	0.92



Figure 54: Overall survival 1984-2003 by FIGO stage







Figure 56: Overall survival 1984-2003 by presentation period

Figure 57: Relapse free survival 1984-2003 by treatment for relapse





Figure 58: Overall survival 1984-1993 by FIGO stage







Figure 60: Relapse free survival 1984-1993 by FIGO stage







Figure 62: Salvage survival 1984-2004 by site of relapse

Figure 63: Salvage survival 1984-2004 by treatment type for relapse



Interpretation of results

Table 17 shows the key characteristics of all those patients who were treated for vaginal cancer at QCGC. We have grouped patients into two categories based on the year in which they presented (1984 to 1993 and 1994 to 2003). All the key characteristics (age, FIGO staging, tumour morphology, and treatment modality) between these two groups were similar, with the exception of tumour grade/differentiation.

Table 18 shows five-year disease specific survival estimates and 95% confidence intervals. Overall 5 year survivals (95% Cl) for the presentation periods 1984 to 1993 and 1994 to 2003 were 53% (41-65) and 53% (39-66) respectively. These differences were not statistically significant.

Tables 19 and 20 show univariate and multivariate Cox proportional hazards models respectively, evaluating the significance of prognostic factors such as age, FIGO stage, treatment time-period, morphology, grade and treatment modality.

Figures 54 and 55 show overall and relapse-free survival between 1984 and 2003, by FIGO stages. Overall survival (95% CI) and relapse-free survival (95% CI) at 192 months/16 years were 47% (36-57%) and 45% (35-54%) respectively. Figures 56 and 57 show overall and relapse-free survival at five years, by presentation period. No significant differences by presentation period could be noticed. Figures 58 to 61 show overall and relapse-free survival by FIGO stages and by presentation period. Figures 62 and 63 show salvage survival for vaginal cancer, by site of relapse and by treatment modality, respectively. The overall salvage survival at five years was 13%.

Table 21: Patient characteristics

Presentation period 1984-2003 (N=560).

		1984-1993	1994-2003	
Factor		N=196 (%)	N=364 (%)	p-value
FIGO stage	I	78 (40)	176 (48)	
	II	58 (30)	46 (13)	
	III	30 (15)	57 (16)	<0.001**
	IV	19 (10)	27 (7)	
	Unknown	11 (5)	58 (16)	
Morphology	SCC	158 (81)	292 (80)	
	Basal cell	5 (3)	13 (4)	
	Paget's disease	5 (3)	22 (6)	<0.001**
	PigNev	5 (3)	24 (7)	
	Other	23 (12)	13 (4)	
Differentiation	Well	49 (25)	82 (23)	
	Moderate	35 (18)	127 (35)	<0.001**
	Poor	17 (9)	43 (12)	
	Other/unknown	95 (48)	112 (31)	
Age (years)	< 30	3 (2)	2 (1)	
	30-39	15 (8)	24 (7)	
	40-49	16 (8)	47 (13)	
	50-59	19 (10)	56 (15)	0.18
	60-69	38 (19)	59 (16)	
	70-79	57 (29)	101 (28)	
	80+	48 (24)	75 (21)	
Treatment modality	Sx alone	149 (76)	287 (79)	
	RT alone	8 (4)	6 (2)	
	C alone	o (o)	o (o)	
	Sx+RT	18 (9)	43 (12)	
	RT+C	10 (5)	8 (2)	0.28
	Sx+C	1 (0)	1 (0)	
	Sx+RT+C	6 (3)	12 (3)	
	Other	4 (2)	7 (2)	Deel
				Page 65

Table 22: Kaplan and Meier Disease Specific Survival (DSS) estimates and 95% confidence intervals

Presentation Period 1984-2003.

E.g. (5/10/16) year (DSS) estimate x% [95% CI].

Period	1984-1993	1994-2003
5 year	82.3[76.7,87.9]	82.0[77.6,86.4]
10 year	77.1[70.7,83.6]	81.1[76.4,85.8]
16 year	73.5[66.1,80.8]	_

FIGO stage	1	П	Ш	IV
5 year	97.0[94.5,99.3]	81.0[73.0,89.0]	62.0[50.2,73.6]	38.0[21.6,54.2]
10 year	90.3[84.5,96.1]	79.5[71.1,87.9]	58.9[46.3,71.4]	37.9[21.6,54.2]
16 year	87.8[80.5,95.2]	70.8[57.1,84.5]	-	-

Morphology	SCC	BCC+Paget's disease	PigNev	Other
5 year	83.1[79.4,86.9]	94.4[83.9,100]	46.0[22.1,69.9]	78.7[64.5,92.8]
10 year	78.4[73.5,83.3]	_	_	-
16 year	75.6[69.5,81.6]	-	-	67.4[43.7,91.1]

Differentiation	Well	Moderate	Poor	Other
5 year	96.1[92.7,99.5]	80.3[73.6,87.0]	70.8[58.1,83.4]	76.9[70.4,83.4]
10 year	94.2[89.2,99.1]	73.7[69.4,82.5]	67.1[53.2,81.0]	73.8[66.3,81.4]
16 year	83.5[68.5,98.3]	_	53.6[27.6,79.7]	-

Age (years)	<40	40-59	60-69	70+
5 year	92.6[84.5,100.0]	87.9[81.8,94.0]	84.8[77.4,92.2]	76.1[70.6,81.7]
10 year	88.2[76.7,99.6]	82.8[73.5,92.1]	81.0[72.2,89.7]	72.7[66.1,79.3]
16 year	-	78.2[65.8,90.6]	-	66.1[55.5,76.7]

Treatment	RT alone	Sx alone	Sx+RT	RT+C	Sx+RT+C
5 year	90.1[87.0,93.2]	42.9[11.7,73.9]	64.7[51.1,78.4]	45.4[21.1,69.8]	48.6[24.8,72.4]
10 year	85.6[91.1,90.1]	_	_	_	24.3[0,60.0]
16 year	84.2[78.9,79.4]	_	45.3[20.3,70.4]	_	_

Table 23: Univariate Cox model

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	Ш	3.99	[2.0,7.96]	<0.001**	2.61	[1.68,4.06]	<0.001**
	ш	9.44	[4.9,18.2]	<0.001**	4.16	[2.66,6.5]	<0.001**
	IV	20.49	[10.3,40.5]	<0.001**	7.65	[4.6,12.6]	<0.001**
Morphology							
SCC vs	BCC	0.34	[0.05,2.39]	0.28	0.61	[0.19,1.9]	0.4
	Paget's disease	0.2	[0.03,1.29]	0.09	1.29	[0.68,2.45]	0.44
	PigNev	3.05	[1.66,5.62]	<0.001**	2.75	[1.6,4.7]	<0.001**
	Other	1.18	[0.57,2.45]	0.65	0.96	[0.52,1.77]	0.89
Period							
1984-1993 vs	1994-2003	0.94	[0.62,1.42]	0.78	0.94	[0.69,1.29]	0.72
Differentiation							
Well vs	Moderate	3.83	[1.79,8.2]	<0.001**	2.32	[1.4,3.8]	<0.001**
	Poor	6.41	[2.8,14.7]	<0.001**	3.57	[2.0,6.36]	<0.001**
	Other	3.89	[1.85,8.2]	<0.001**	2.53	[1.56,4.08]	<0.001**
Age							
<40 years vs	40-59	1.5	[0.51,4.4]	0.46	1.24	[0.56,2.7]	0.6
	60-69	2.04	[0.69,6.05]	0.2	1.98	[0.9,4.3]	0.08
	70+	3.17	[1.2,8.6]	0.02*	2.63	[1.28,5.4]	0.009**
Treatment							
RT vs	Sx	0.11	[0.05,0.25]	<0.001**	0.21	[0.1,0.43]	<0.001**
	RT+Sx	0.41	[0.17,0.99]	0.05*	0.54	[0.24,1.18]	0.12
	RT+C	0.82	0.31,2.21]	0.7	0.66	[0.25,1.7]	0.39
	Sx+RT+C	0.85	[0.32,2.23]	0.73	0.83	[0.33,2.07]	0.7
	Other	1.81	[0.66,5.0]	0.25	2.19	[0.82,5.8]	0.12

Table 24: Multivariate Cox model

Factor			DSS			RFS	
		Hazard	[95% CI]	p-value	Hazard	[95% CI]	p-value
Stage							
l vs	II	2.92	[1.42,6.04]	<0.001 **	2.06	[1.29,3.29]	<0.001**
	ш	5.46	[2.5,11.67]	<0.001 **	2.72	[1.59,4.64]	<0.001**
	IV	7.48	[3.3,16.9]	<0.001 ^{**}	3.81	[2.07,7.02]	<0.001**
Morphology							
SCC vs	BCC	0.22	[0.03,1.8]	0.28	0.63	[0.18,2.2]	0.47
	Paget's disease	0.13	[0.01,1.2]	0.09	1.6	[0.55,4.6]	0.38
	PigNev	1.61	[0.57,4.5]	<0.001**	3.29	[1.38,7.87]	0.007**
	Other	1.24	[0.55,2.8]	0.65	1.09	[0.56,2.12]	0.8
Period							
1984-1993 vs	1994-2003	1.26	[0.79,2.02]	0.78	1.07	[0.76,1.52]	0.69
Differentiation							
Well vs	Moderate	2.33	[1.05,5.2]	<0.001 **	1.73	[1.03,2.91]	0.04*
	Poor	2.72	[1.14,6.48]	<0.001 **	2.0	[1.09,3.66]	0.02*
	Other	2.96	[1.28,6.8]	<0.001 **	1.95	[1.13,3.38]	0.02*
Age							
<40 years vs	40-59	1.65	[0.54,5.1]	0.46	1.12	[0.51,2.46]	0.79
	60-69	1.79	[0.58,5.52]	0.2	1.63	[0.74,3.6]	0.23
	70+	2.47	[0.85,7.2]	0.02*	1.92	[0.92,4.02]	0.08
Treatment							
RT vs	Sx	0.41	[0.16,1.05]	<0.001 ^{**}	0.55	[0.23,1.27]	0.16
	RT+Sx	0.6	[0.24,1.53]	0.05*	0.79	[0.34,1.84]	0.59
	RT+C	1.1	[0.39,3.1]	0.7	0.86	[0.32,2.34]	0.76
	Sx+RT+C	1.6	[0.56,4.52]	0.73	1.41	[0.54,3.68]	0.49
	Other	2.09	[0.64,6.86]	0.25	2.43	[0.83,7.12]	0.1



Figure 64: Overall survival 1984-2003 by FIGO stage







Figure 66: Overall survival 1984-2003 by presentation period

Figure 67: Relapse free survival 1984-2003 by presentation period




Figure 68: Overall survival 1984-1993 by FIGO stage







Figure 70: Relapse free survival 1984-1993 by FIGO stage







Figure 72: Salvage survival 1984-2003 by site of relapse





Interpretation of results

Table 21 shows key characteristics of patients diagnosed with vulval cancer by presentation period. Age grouping and treatment modality were similar between the two groups. However, there were significant differences in FIGO stages, tumour morphology and differentiation.

Table 22 shows disease specific survival estimates and 95% confidence intervals. Overall five-year survivals were similar between the presentation periods. Tables 23 and 24 show univariate and multivariate Cox proportional hazards models respectively, evaluating the significance of prognostic factors such as age, FIGO stage, treatment time-period, morphology, grade and treatment modality.

Figures 64 and 65 show overall and relapse-free survival between 1984 and 2003, by FIGO stages. Overall survival (95% CI) and relapse-free survival (95% CI) at 192 months/16 years were 74% (69-80%) and 60% (54-65%) respectively. Figures 66 and 67 show overall and relapse-free survival at five years by presentation period. Survival curves were similar between the presentation periods. Figures 68-71 show overall and relapse-free survival by presentation period and FIGO stages. Figures 72 and 73 show five-year salvage survival curves by site of relapse and by treatment modality. Between 1982 and 2003, the overall salvage survival (95% CI) at five years was 47% (37-57%).

Appendix 1: Glossary

AdenoCa	adenocarcinoma
AdenoSq	adenosquamous carcinoma
Any dist	any distant relapse
BCC	basal cell carcinoma
С	chemotherapy
CI	confidence interval
CS	carcinosarcoma
DSS	disease specific survival
Endometrioid	endometrioid adenocarcinoma
FIGO	International Federation of Gynecology and Obstetrics
LMS	leiomyosarcoma
LR	loco-regional relapse
Meso	mesodermal mixed tumour
Mucinous	mucinous adenocarcinoma
Mull	mullerian mixed tumour
PigNev	pigmented nevus
QCGC	Queensland Centre for Gynaecological Cancer
QCR	Queensland Cancer Registry
R	radiotherapy
Rel	relapse
RFS	relapse free survival
RT	radiotherapy
S1	stage I
S2	stage II
S3	stage III
S4	stage IV
SCC	squamous cell carcinoma
Ser/PapSer	serous/papillary serous
Sx	surgery

Notes