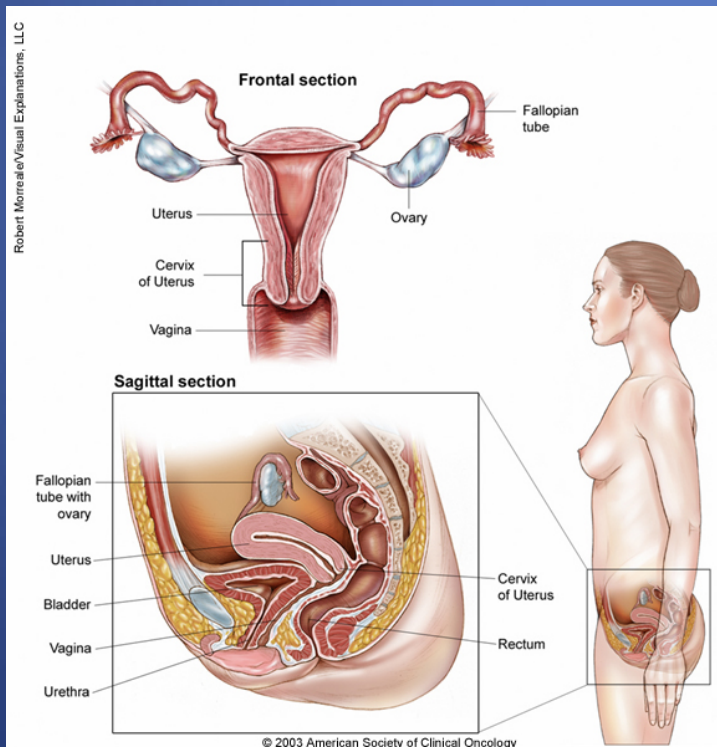


Ovarian Cancer

Josie Rutovitz



NORTHERN HAEMATOLOGY & ONCOLOGY GROUP



Extent of the Problem

- In 2006 = 9th most common cancer in women (Aust Institute of Health and Welfare).
- 1226 new cases in 2006.
- 60% of cases are post-menopausal.
- 47% increase in incidence from 1982 – 2006 (Partly due to aging of the population.).
- 60% are under age 60 and a further 7% are under age 40.

- 795 patients died of Ovarian cancer in 2006.
- 6th most common cause of cancer deaths and the cause of 55% of Gynaecological cancer deaths.
- 5 year survival rate across all age groups is about 40%.

Table 2.1: Incidence of the 10 most commonly diagnosed cancers^(a), females, 2006

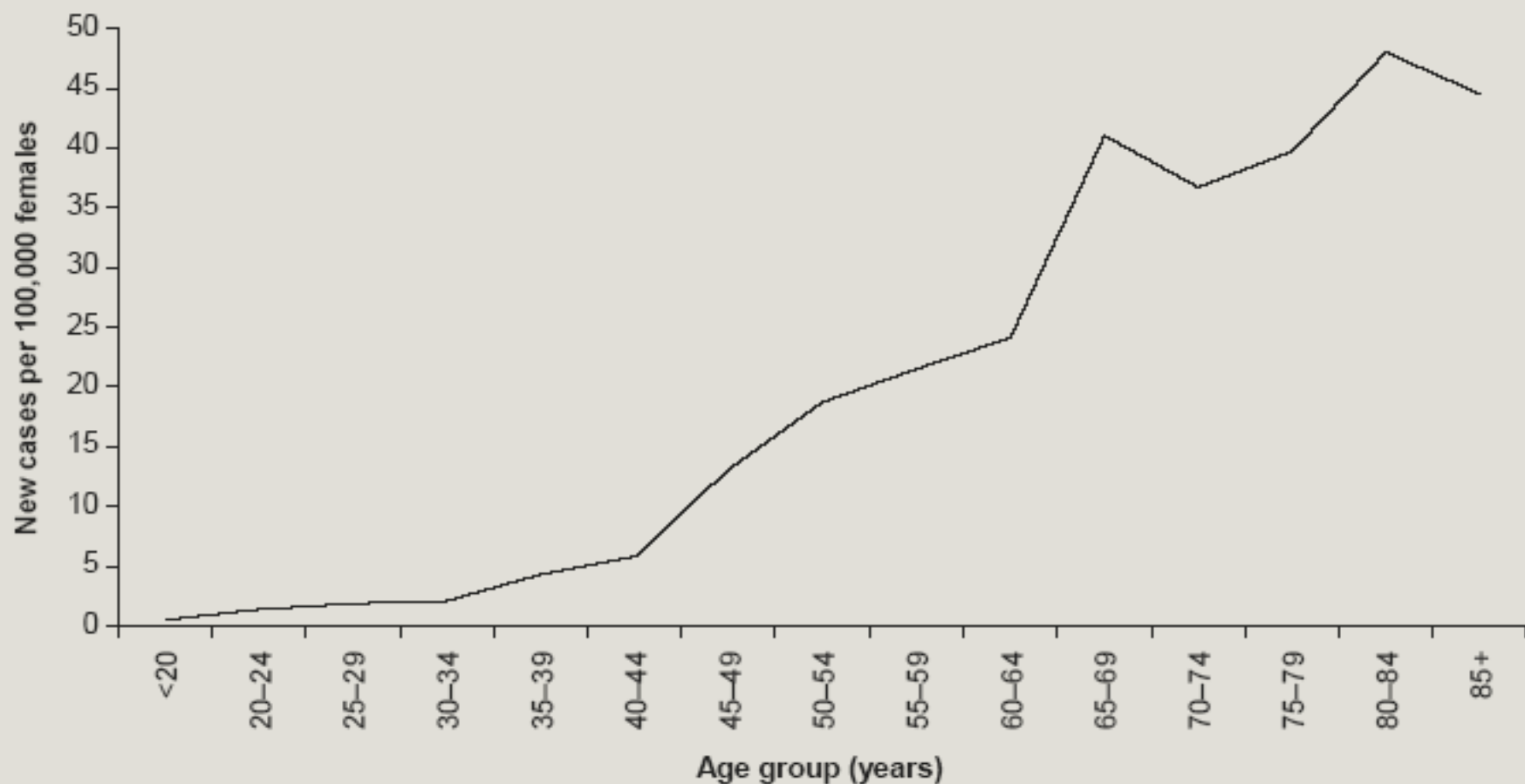
Cancer type (ICD-10 codes)	Number of cases	Per cent of all gynaecological cancer cases	Per cent of all cancer cases ^(a)	Age-standardised rate ^(b)	95% confidence interval
Breast (C50)	12,614	..	27.7	112.4	110.4–114.4
Bowel (C18–C20)	6,159	..	13.5	52.1	50.8–53.4
Melanoma of skin (C43)	4,275	..	9.4	38.2	37.1–39.4
Lung (C33–C34)	3,533	..	7.8	30.3	29.3–31.3
Lymphoma (C81–C85, C96)	1,961	..	4.3	17.2	16.4–18.0
Uterus (C54, C55)	1,860	43.8	4.1	16.3	15.6–17.1
Unknown primary site (C26, C39, C76, C80)	1,592	..	3.5	12.6	12.0–13.3
Thyroid (C73)	1,270	..	2.8	11.8	11.2–12.5
Ovary (C56)	1,226	28.9	2.7	10.7	10.1–11.4
All leukaemias (C91–C95)	1,111	..	2.4	9.7	9.1–10.3
All cancers^(c)	45,534	..	100.0	396.3	392.6–400.0

(a) Excluding basal and squamous cell carcinomas of the skin.

(b) The age-standardised rates were standardised to the Australian population as at 30 June 2001 and are expressed per 100,000 females.

(c) Includes cancers coded in ICD-10 as C00–C97, D45, D46, D47.1 and D47.3 with the exception of those C44 codes which indicate a basal or squamous cell carcinoma.

Source: Australian Cancer Database, AIHW.

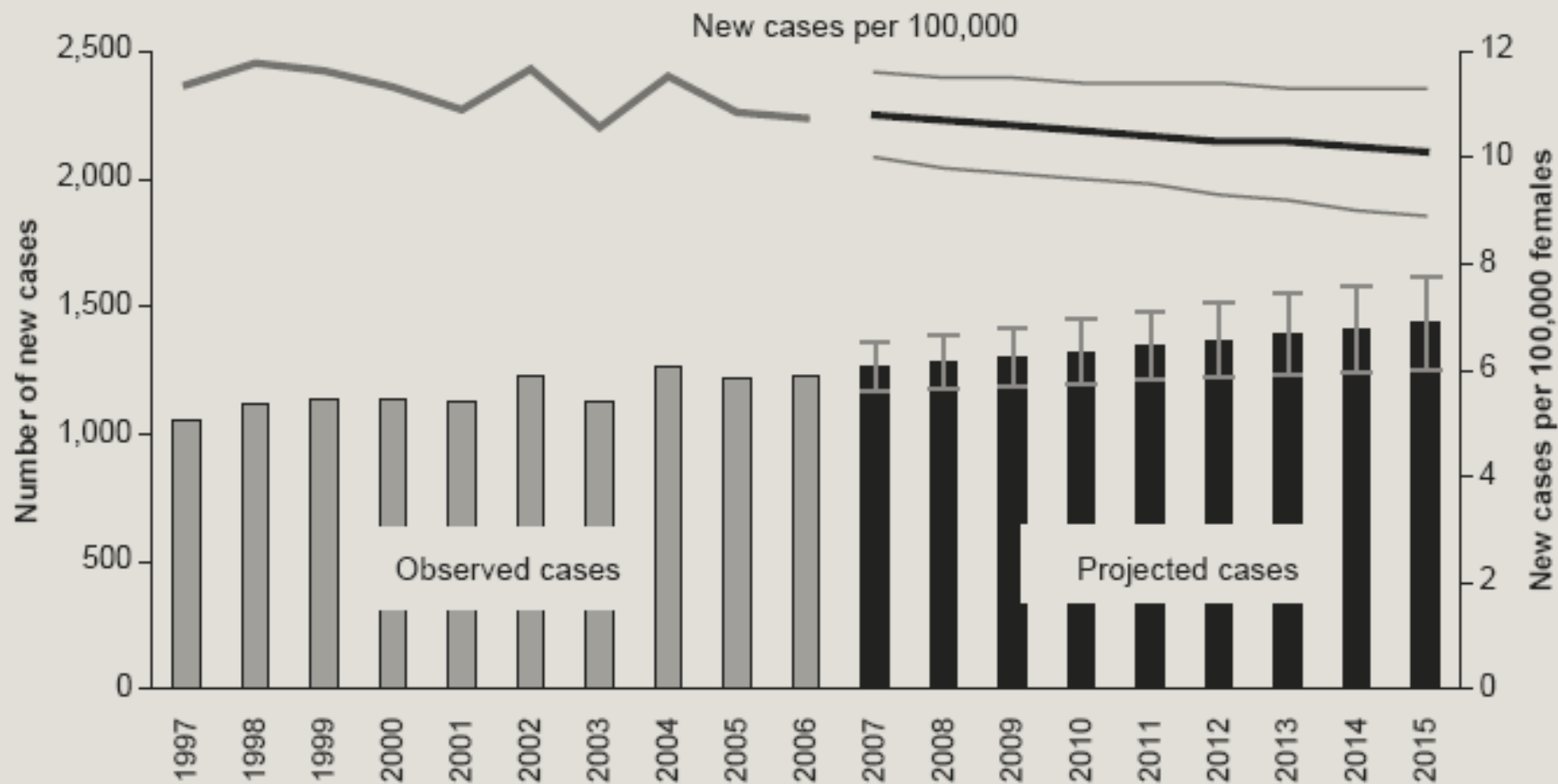


Notes

1. The rates shown are age-specific rates.
2. The data for this figure are shown in Appendix Table D2.1.

Source: Australian Cancer Database, AIHW.

Figure 2.1: Incidence of ovarian cancer by age at diagnosis, 2006



Notes

1. The projections were based on ovarian cancer incidence data for 1997 to 2006.
2. The rates were age-standardised to the Australian population as at 30 June 2001.
3. For the years 2007 to 2015, grey lines around the age-standardised rates indicate the 95% prediction intervals.
4. The data for this figure are shown in Appendix Tables D2.2 and D2.4.

Source: Australian Cancer Database, AIHW.

Figure 2.4: Incidence of ovarian cancer, observed for 1997 to 2006 and projected for 2007 to 2015

Table 3.1: The 10 most common types of cancer deaths, females, 2006

Cancer type (ICD-10 codes)	No. of deaths	% of all gynaecological cancer deaths	% of all cancer deaths	% of all deaths	ASR ^(a)	95% confidence interval
Lung (C33–C34)	2,683	..	15.7	4.1	22.7	21.8–23.6
Breast (C50)	2,618	..	15.3	4.0	22.1	21.3–23.0
Unknown primary site (C26, C39, C76–C80)	1,917	..	11.2	2.9	15.1	14.5–15.8
Bowel (C18–C20)	1,675	..	9.8	2.6	13.6	12.9–14.2
Pancreas (C25)	1,029	..	6.0	1.6	8.4	7.9–8.9
Ovary (C56)	795	54.7	4.6	1.2	6.7	6.2–7.2
All lymphomas (C81–C85, C96)	669	..	3.9	1.0	5.4	5.0–5.8
All leukaemias (C91–C95)	609	..	3.6	0.9	5.0	4.6–5.4
Melanoma (C43)	452	..	2.6	0.7	3.8	3.5–4.2
Stomach (C16)	448	..	2.6	0.7	3.6	3.3–4.0
All cancers^(b)	17,123	..	100.0	26.3	141.0	138.9–143.2

(a) The age-standardised rates were standardised to the Australian population as at 30 June 2001 and are expressed per 100,000 females.

(b) Includes cancers coded in the ICD-10 as C00–C97, D45, D46, D47.1 and D47.3.

Source: National Mortality Database, AIHW.

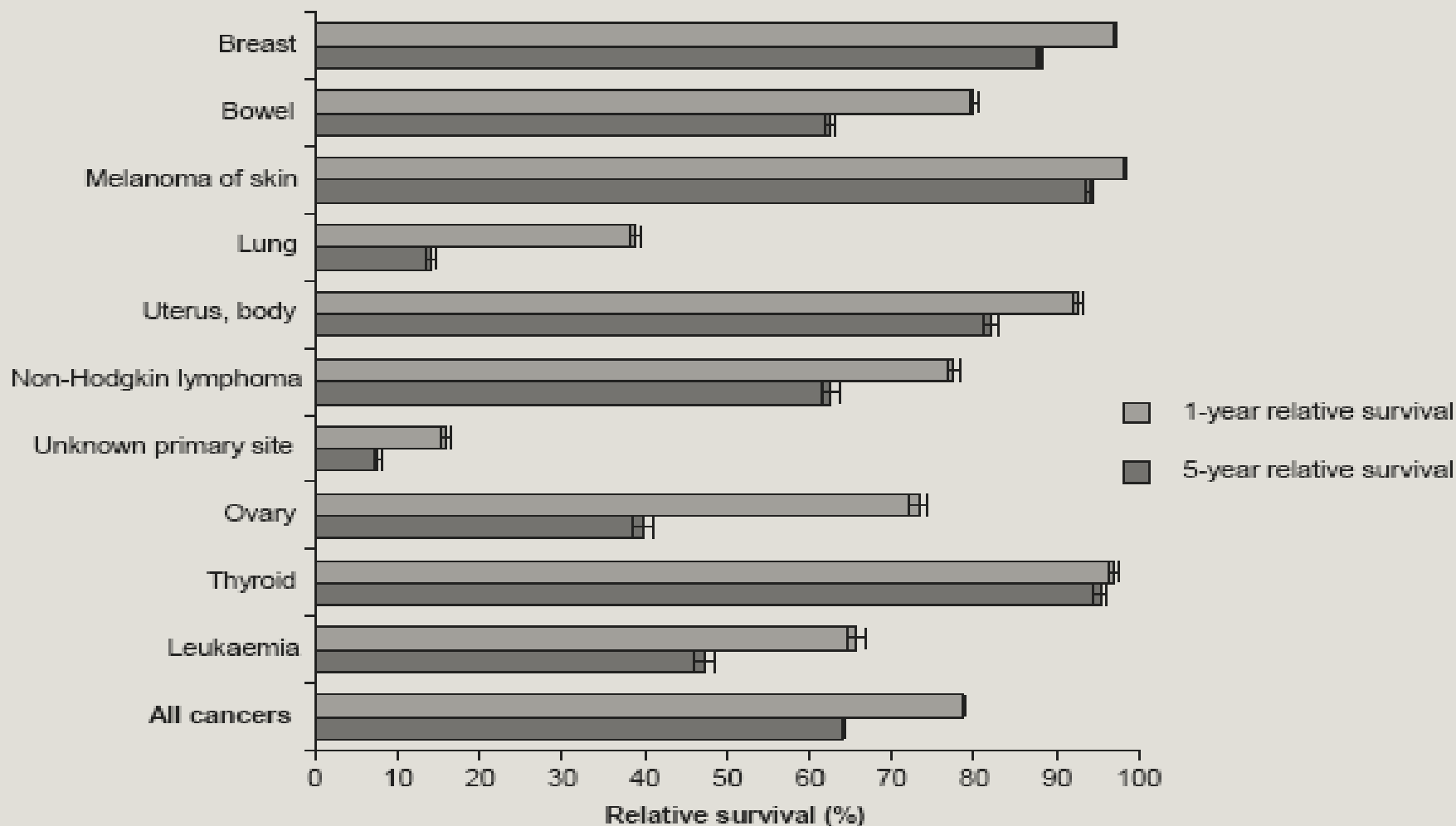


Notes

1. The rates shown are age-specific rates.
2. The data for this figure are shown in Appendix Tables D2.1 and D3.1.

Source: Australian Cancer Database, AIHW & National Mortality Database, AIHW.

Figure 3.1: Ovarian cancer incidence and mortality by age group, 2006



Notes

1. The most commonly diagnosed cancers, excluding non-melanoma skin cancer (C44), were determined using data for 2004; the cancers have been listed in order of how common they were.
2. 'All cancers' includes cancers coded in ICD-10 as C00–C97 (except for C44), D45, D46, D47.1 and D47.3.
3. The data for this figure are shown in Appendix Table D4.1.

Source: AIHW, CA & AACR 2008; Australian Cancer Database, AIHW.

Figure 4.1: Relative survival, 10 most commonly diagnosed cancers, females, 1998–2004

Risk Factors

- Age
 - Obesity BMI > 30
 - Nulliparity
 - First child at age older than 30
 - Fertility drugs (Clomid) use for longer than 1 year
 - Androgen usage (Danazol)
 - Oestrogen only HRT
 - Family history (BRCA 1/2)
 - Personal history of breast cancer
-
- Tubal ligation reduces risk by 67%
 - Hysterectomy (but not ovaries) reduces risk by 30%
 - OCP is protective - use for 3 years plus reduces by 30-50%
 - Low fat diet protects

Symptoms

- Non-specific
- Bloating
- Pelvic pain
- Early satiety
- Urinary frequency
- Fatigue
- Pain with intercourse
- Back pain
- Constipation

Diagnosis

- High index of suspicion.
- CA-125 – suggestive but not diagnostic (except at high levels.)
- Trans-vaginal ultrasound
- Biopsy

Staging

- Mostly done at the time of surgery
- Use TNM classification
- **Stage I:** This stage describes cancer that is located only in the ovaries (T1, N0, M0).
 - Stage IA: The cancer is encapsulated and is located in only one ovary with no spread to pelvic lymph nodes or other parts of the body (T1a, N0, M0).
 - Stage IB: The cancer is encapsulated and is located in both ovaries with no spread to pelvic lymph nodes or other parts of the body (T1b, N0, M0).
 - Stage IC: The cancer is in one or both ovaries with either a ruptured capsule or tumour spread to the ovarian surface or cancerous cells in the abdominal fluid (T1c, N0, M0).

- **Stage II:** The cancer is in one or both ovaries and has grown into the pelvis (T2, N0, M0).
 - Stage IIA: The cancer has grown into the uterus or fallopian tubes, but not to the pelvic lymph nodes or distant organs (T2a, N0, M0).
 - Stage IIB: The cancer has spread to other pelvic tissue, but not to lymph nodes or distant organs (T2b, N0, M0).
 - Stage IIC: The cancer has spread into the pelvic area and is shedding cancer cells into the abdominal fluid (T2c, N0, M0).

- **Stage III:** The cancer is located in one or both ovaries and the pelvis and has spread into the peritoneum (T3, N0, M0).
 - Stage IIIA: The cancer has spread microscopically throughout the pelvis (T3, N0, M0).
 - Stage IIIB: The cancer has spread into the peritoneal area with areas of tumor growth that are 2 cm or smaller (T3b, N0, M0).
 - Stage IIIC: This stage describes any cancer that has spread into the peritoneal area with areas of tumor growth larger than 2 cm (T3c, N0, M0). Or, the cancer has spread to the lymph nodes and/or pelvis, but not to other parts of the body (any T, N1, M0)
- **Stage IV:** This stage describes any cancer that has spread to distant organs (any T, any N, M1).

Stage	Relative 5-Year Survival Rate
Stage I	89%
IA	94%
IB	91%
IC	80%
Stage II	66%
IIA	76%
IIB	67%
IIC	57%
Stage III	34%
IIIA	45%
IIIB	39%
IIIC	35%
Stage IV	18%

Treatment

- Primary treatment is surgical debulking.
 - Gynaecological Oncologist
 - Extent of residual disease correlates with survival
 - In stage IV disease, median survival is an average of 10 months longer for residual tumour bulk being less than 2cm compared to greater.
- Chemotherapy
 - Multiple agents
 - Intravenous
 - Intraperitoneal
 - Newer agents
- Radiotherapy – whole abdomen

- Mainstay of chemotherapy is combination treatment (polychemotherapy).
 - Taxanes and platinum
 - Variable data of paclitaxel vs. Docetaxol
 - One of the few tumour types where carboplatin has replaced cisplatin
- Some trials suggest single agent carboplatin is equivalent
 - Use in maximal doses
 - Older, more frail patients
 - SCOTROC trials
- Older protocols include carboplatin and cyclophosphamide
- Some protocols call for interim or second look laparotomy

- Relapsed disease.
 - If possible, try resection.
- Time to relapse is important
 - Platinum resistance defined as relapse within 6 months.
- Retreat with chemotherapy
 - Single agent treatment
 - Taxanes
 - Platinum
 - Caelyx (pegalated doxorubicin)
 - Topotecan
 - Etoposide
 - Chlorambucil
 - Irinotecan

Intraperitoneal treatment

- Strong proponents and opponents.
- No clear data.
- Only about 5mm penetration of intraperitoneal chemotherapy into tissue.
- Only suitable for optimally debulked patients.
- TRIPOD - Trial of Intraperitoneal Chemotherapy with Paclitaxel and Cisplatin after Optimal Debulking Surgery for Ovarian and Related Cancers.
- Combination of
 - IV paclitaxel
 - IP carboplatin
 - IP paclitaxel
- Requires the surgical placement of a “Port”.

Newer agents

- Vascular Endothelium Growth Factor Receptor Antagonist (VEGFR blocker)
 - Bevacizumab (Avastin)
 - cedaranib
- Improved disease free progression
- No impact yet on overall survival
- Dramatic results in improving ascites and pleural effusions
- Expensive ++++ - about \$60,00 a year

Follow Up

- CA-125
 - Useful monitoring tool but;-
 - Not a diagnostic test
 - Picks up pre-clinical disease
 - No proof that treating a serological relapse improves survival in the absence of clinical disease
 - Significant impact on quality of life
- CT scan
 - Often negative in relapsed ovarian carcinoma.
 - Peritoneal disease not easily seen.
- PET scans
 - Very sensitive tool
 - Can confirm a suspected relapse but does not change prognosis
- Clinical examination
 - Probably least sensitive but most appropriate method

Long Term Toxicity

- Up to 40% of patients can have ongoing fatigue.
- Platinum analogues can cause high tone hearing loss
- Peripheral neuropathy (taxanes)
- Anaemia
- Neutropaenia
- Anxiety