The New South Wales Colorectal Cancer Care Survey 2000
Part 2 - Chemotherapy Management

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Summary

The primary aim of the New South Wales (NSW) Colorectal Cancer Care Survey was to determine the proportion of colorectal cancer cases in NSW managed according to recommendations in the National Health and Medical Research Council (NHMRC) guidelines for the prevention, early detection and management of colorectal cancer (http://www.nhmrc.gov.au/publications/synopses/cp62syn.htm). These guidelines had been released and widely disseminated to practitioners involved in the management of patients with colorectal cancer, including surgeons and radiation and medical oncologists in Australia, before commencement of the survey.

Information was sought from primary treating practitioners regarding their management of patients newly diagnosed with colorectal cancer who were notified to the NSW Central Cancer Registry between 1 February 2000 and 31 January 2001; 94% of the 3377 patients ascertained were diagnosed in 2000, 2% in 1999 and 4% in 2001. This report covers their initial chemotherapy management. A previous report described the surgical management of these patients.[1]

Data on chemotherapy treatment were obtained on 809 (88%) of 920 patients in this survey who received chemotherapy as part of their initial treatment. Assessment of chemotherapy management with reference to the guidelines was limited to 778 patients who had only one primary cancer diagnosed.

Concordance of management with NHMRC guidelines is summarised below for the recommendations relating to chemotherapy management.

NHMRC Guideline	**Management**
Adjuvant chemotherapy for colon cancer	
People with resected node-positive colon cancer should be offered adjuvant therapy. (Level I evidence)	59% of patients who had resection for a node-positive bowel cancer received adjuvant chemotherapy; another 16% were considered for the treatment, but did not receive it (Table 46 of surgical report [1]).
*Treatment should start within five weeks of surgery (the standard in most studies). (Expert opinion)	52% of patients started chemotherapy within six weeks of surgery (Table 16).
5-FU plus low-dose leucovorin for six months is the preferred option. Other adjuvant therapy regimens with similar reductions in the rate of relapse and mortality (30–40%) include: • 5-FU plus low-dose leucovorin ± levamisole for six months; and • 5-FU plus levamisole for one year. (Level II evidence)	5-FU plus low dose leucovorin was given to 82% of patients. Of these patients, 95% received the treatment for six months (Table 17).

Adjuvant chemotherapy for rectal cancer	
Postoperative 5-FU based chemotherapy and radiotherapy (combined modality therapy) is recommended for patients with high-risk rectal cancer. (Level II evidence)	13% of patients with tumours that had penetrated beyond the full thickness of the bowel wall or involved regional nodes received postoperative combined modality therapy. Another 12% of these patients received combined modality therapy based on preoperative radiotherapy (Table 54 of surgical report [1]).
When chemotherapy is given postoperatively in combination with radiotherapy, protracted venous infusion of 5-FU chemotherapy may offer further benefits in survival when compared to bolus 5-FU therapy. It is the recommended way of delivering combined modality therapy. (Level II evidence)	59% of patients who received 5-FU concurrently with radiotherapy had this administered by continuous infusion during the combined modality phase (page 26).
Management of metastatic colorectal cancer	
First-line 5-FU-based chemotherapy prolongs life when compared to best supportive care and should be offered to patients with advanced colorectal cancer. (Level II evidence) The timing of commencement of chemotherapy in asymptomatic patients is unclear, although one study suggests it is best administered early. (Level II evidence)	52% of patients with Stage IV colon cancer and 58% of patients with Stage IV rectal cancer received chemotherapy (Tables 48 and 54 of surgical report [1]).
5-FU plus leucovorin, 5-FU plus methotrexate, and continuous infusion 5-FU are all associated with an improvement in response rate over 5-FU alone. Survival advantages in the palliative setting may exist, but are small with no clear quality-of-life benefits over 5-FU alone. (Level I evidence)	74% of patients who underwent chemotherapy for Stage IV disease received 5-FU plus leucovorin (Table 22).
Participation in clinical trials	
Doctors should encourage patients with colorectal cancer to consider participating in appropriate clinical trials for which they are eligible. (Expert opinion)	46% of patients were treated by medical oncologists who were not taking part in any trials. 12% were considered to be eligible for a trial and 8% were participating in one.

Follow-up intentions	
All patients who have undergone surgery for colorectal cancer should have specialist follow-up in conjunction with the patient's general practitioner. (Expert opinion)	For 68% of patients who had chemotherapy, their medical oncologist intended to be involved in their follow-up (Table 25).

*Endorsed as a recommendation by the survey's Expert Advisory Group but not covered in the NHMRC guidelines.

Generally, there was a reasonable degree of concordance between medical oncology practice for colorectal cancer in NSW in 2000 and important recommendations in the NHMRC guidelines pertaining to the choice of chemotherapy regimen used, and duration of adjuvant chemotherapy. On the other hand, nearly half the patients in this survey started adjuvant chemotherapy more than six weeks from the date of surgery. Timeliness in commencing adjuvant postoperative chemotherapy is considered to be an important factor for its effectiveness; hence the results indicate there is scope for improvement in this aspect of colorectal cancer management. Factors that may cause this delay include waiting times to see a medical oncologist and to start chemotherapy, and to a lesser extent post-surgical problems. Referral to a medical oncologist at an earlier stage, eg as soon as the pathology results are available in the surgical ward rather than following hospital discharge, may improve this aspect of chemotherapy management. As previously reported, the number of people with resected node-positive colon cancer (Level I evidence) and the number of people with high-risk rectal cancer (Level II evidence) who were offered adjuvant therapy, was suboptimal (pages 45 and 48 of surgical report[1]).

More effective and rapid uptake of evidence into the management and treatment of colorectal cancer might be achieved through regular review and updating of the NHMRC guidelines. This should be supported by more organised and active steps of professional organisations, health services and the Cancer Institute NSW to ensure that guidelines are communicated to medical oncologists in ways that have been shown to influence practice.

Background

Australia has one of the highest incidence rates of colorectal cancer in the world. In 2000 there were 12,405 new cases and 4718 deaths from the disease.[2] Important advances in the last decade such as the use of "adjuvant" postoperative chemotherapy have allowed for significant improvement in its outcomes.[3,4]

Comprehensive guidelines on the management of colorectal cancer were developed by the Clinical Oncological Society of Australia (COSA) in conjunction with the Australian Cancer Network (ACN). The guidelines were then endorsed by the NHMRC and released in late 1999. All surgeons and oncologists in Australia were sent a copy of these guidelines.[5] They are available at http://www.nhmrc.gov.au/publications/synopses/cp62syn.htm.

The availability of such a document defining "best practice" management is an important first step towards attaining optimal care, however there is evidence that dissemination of guidelines without rigorous active implementation has not always met with success in improving practice.[6]

Colorectal cancer audits to date indicate that there are substantial variations between practitioners in outcomes for rectal cancer. An audit of 645 patients in Glasgow revealed wide differences in outcomes such as anastomotic leakage (0-25%), postoperative mortality (0-20%) and 10-year survival (20-63%) between 13 surgeons.[7] Two large studies, in Britain and Germany, found as much as a 10-fold difference in recurrence rates for rectal cancer between individual surgeons. These individual differences remained statistically significant after adjusting for other prognostic variables.[8,9] Differences in practice possibly account for this variation.

In 1990 a United States National Cancer Institute (NCI) consensus conference recommended adjuvant chemotherapy as the standard of care for patients with resected Stage III (Dukes C) colon cancer.[10] A report published in 1999, on 477 patients admitted to a community-based Australian hospital between 1989 and 1994, found that only 5% of patients with Dukes C colon cancer commenced adjuvant chemotherapy, and only 3% completed a course.[11]

Given the evidence indicating significant variation in colorectal cancer treatments and outcomes, together with the availability of a defined standard of care and difficulties with the implementation of clinical management guidelines, it was considered timely to obtain a baseline record of existing management practices and outcomes for this disease in NSW in 2000.

Some of the data from the NSW survey contributed to the National Colorectal Cancer Care Survey which was conducted on all newly-diagnosed colorectal cancer patients notified to each Australian Cancer Registry between 1 February and 30 April 2000.[12] This survey showed among other things, that there was less than 50% concordance of treatment with eight of the 23 NHMRC guidelines analysed. Variations in the types of operation performed, participation in clinical trials, and the use of adjuvant therapy (which varied by patient's age) were also observed. In relation to the NCI's recommendation, 76% of patients with Stage C colon cancer were offered chemotherapy, with 64% of patients with Stage C colon cancer receiving it.

Coverage

This report describes the initial treatment of colorectal cancer (excluding carcinoma in-situ) in NSW, Australia, predominantly in the year 2000. All detailed analyses are based on patients who had only one primary colorectal cancer treated in the episode of care that was surveyed. Most analyses include only patients who had chemotherapy.

Aims

The aims of the NSW Colorectal Cancer Care Survey were to obtain a comprehensive record of the management and outcomes of patients with newly diagnosed colorectal cancer in NSW in 2000. The survey sought to determine:

1. The proportion of colorectal cancer cases in NSW managed according to recommendations in the NHMRC guidelines.

2. The variables relating to the patient, their cancer and their doctor, that are associated with management that is in accordance with guideline recommendations.

3. The two-year disease-free survival and overall survival rates for the patients studied.

4. The level of concordance with the guidelines and how this relates to recurrent disease and cancer-specific and overall survival for this cohort.

This report addresses points 1 and 2 in relation to chemotherapy management only.

Methods

Questionnaires were designed to record key aspects of the management of colorectal cancer described in the NHMRC guidelines. Separate questionnaires were used to collect information pertinent to chemotherapy (Appendix 1), surgery and radiotherapy. A multidisciplinary Expert Advisory Group of clinicians provided oversight for the development of these questionnaires (Appendix 2). Completion of the questionnaires by practitioners was validated against separate abstraction of information from records in a pilot study.

Patients newly diagnosed with colorectal cancer and notified to the NSW Central Cancer Registry (CCR) between 1 February 2000 and 31 January 2001 were entered into this survey. Patients were excluded if they only had benign tumours, had a previous primary colorectal cancer, were treated outside NSW, or were non-Australian residents.

Practitioners who treated these patients were identified from CCR notifications and were sent the relevant questionnaires seeking information on treatment received within their speciality. The contact details of other practitioners who treated these patients were also requested. The relevant questionnaires were then sent to these practitioners.

Unreturned questionnaires were followed up with reminder letters and phone calls. Field collection was done to abstract information from patients' medical records if a practitioner requested it. Patients were not contacted for this survey.

Data collected were entered in an Access database then analysed using Statistical Analysis System (SAS, Version 8).

Approval for the conduct of this survey was obtained from the Ethics Committees of The Cancer Council NSW and the University of Newcastle. Where necessary, ethics clearance was also obtained from Area Health Services or institutions where field collection was performed.

Scope of this report

This report covers aspects related to the initial chemotherapy management of the cohort. Separate reports will cover the following aspects of colorectal cancer management and outcomes:

- Histopathology reporting
- Surgery (report released April 2004 - http://www.cancercouncil.com.au/editorial.asp?pageid=1021)
- Radiotherapy (in preparation)
- Follow-up investigations and clinical outcomes (in preparation)

Key results from the surgical report regarding chemotherapy treatment are repeated in this report for completeness.[1]

Data Quality

Representativeness of the sample

As this was to be a population based survey it was essential that the cases included in the study were representative of all incident colorectal cancers in NSW during the study period.

Since 1972, notification of malignant neoplasms to the NSW Central Cancer Registry has been a statutory requirement in NSW for all public and private hospitals, pathology laboratories, radiation oncology departments, nursing homes and the Registry of Births, Deaths and Marriages. This has led to the keeping of accurate population statistics for most malignancies. In 2000, 94% of colon cancers and 96% of rectal cancers had histological verification of the disease. As a rough index of the completeness of notification, the proportion of cases in NSW where the only source of notification was from a death certificate was 0.9% for colon and 0.5% for rectal cancers.[13]

The accrual of consecutively notified cases of colorectal cancers for a 12-month period in NSW provides a sample representative of colorectal cases in NSW.

Timeliness of the cohort

Although this survey intended to record the initial management of colorectal cancer newly diagnosed in NSW in 2000, cases were accrued according to the date of first cancer notification at the NSW Central Cancer Registry rather than the date of diagnosis.

The breakdown of all notifications accrued in the survey by date of diagnosis was: 94% of patients diagnosed in 2000, 4% in 2001 and 2% in 1999.

Questionnaire response rate

As reported elsewhere, data were obtained for 3095 (93%) of 3314 questionnaires sent to surgeons.[1] From the data provided by surgeons and Cancer Registry notifications, chemotherapy questionnaires were sent to medical oncologists for 920 patients, of which 809 (88%) were completed (Table 1). This high return rate ensures that the chemotherapy management recorded in the survey is representative of the management of patients with colorectal cancer in NSW.

Cases for which data on chemotherapy management were available and those where data were not were compared on demographic characteristics (Table 2). Patients for whom data were not supplied tended to be somewhat older than those for whom they were supplied.

Validity of chemotherapy questionnaire

Questionnaires used in this survey were designed specifically to record aspects of management covered in the NHMRC guidelines. Performance indicators were developed to measure the conformity of practice to each of the major guideline recommendations. Data items required to construct each performance indicator were then identified. Questions were designed to collect information pertinent to the data items required.

Accuracy of the data collected

A pilot study was performed before commencement of the main survey to test and validate the questionnaires for collecting information on the management of colorectal cancer from patients' treating practitioners. Sixty questionnaires were sent to practitioners in metropolitan Sydney who were identified from an earlier batch of first colorectal notifications received at the NSW Central Cancer Registry. The survey's project coordinator validated data provided from the practitioners by checking the completed forms against information held in patients' hospital or clinic medical records.

The discrepancies found between the questionnaire and patient records were minor and did not indicate that any modifications to the questionnaire would be required.

For the main study, a trained field officer abstracted information from patient records when practitioners were unable to fill in the questionnaires but were willing to provide access to patient records.

Coverage of guideline recommendations

Most recommendations relevant to colorectal cancer management by chemotherapy have been covered in this survey. They span the following topics in the NHMRC guidelines:

- Adjuvant therapy for colon cancer
- Adjuvant therapy for rectal cancer
- Advanced rectal cancer
- The role of systemic chemotherapy (for metastatic colorectal cancer)
- Management of liver metastases

Where sections of the report are relevant to the guidelines they have been stated. When no level of evidence is given it means that the guideline is based on consensus of expert opinion.

Level I	*Evidence obtained from systematic review of all relevant randomised controlled trials.*
Level II	*Evidence obtained from at least one properly designed randomised controlled trial.*
Level III	*Evidence obtained from a well-designed controlled trial without randomisation; or from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group; or from multiple time-series with or without the intervention.*

Results

The data presented in this report reflect the information collected from the chemotherapy questionnaire alone. These forms were only sent to the relevant medical oncologist when a patient was known to have received chemotherapy. The questionnaire's main aims were to obtain details of chemotherapy treatment. Hence this report does not seek to identify the reasons patients did not have chemotherapy, even though this treatment was recommended in the guidelines. Surgeons' referral practices for chemotherapy were described in the surgical report.[1]

Certain details, eg pertaining to tumour stage and treatment modalities received, were collected in all questionnaires. Small differences in these details between this report and the preceding surgical report and succeeding radiotherapy report reflect differences in data provided by different practitioners for the same patient with respect to these overlapping data items.

Characteristics of patients studied

920 of the 3377 patients entered into this survey were identified as having received chemotherapy. Such patients consisted of:

- Eligible notifications to the NSW Central Cancer Registry that indicated that the patient underwent chemotherapy for colorectal cancer, and
- Cases where a practitioner gave details in a surgical or radiotherapy questionnaire of a medical oncology referral or chemotherapy treatment.

Patients who declined the offer of a referral to a medical oncologist, or chose not to receive any chemotherapy despite advice from a medical oncologist, are not included.

As the purpose of this report is to describe chemotherapy treatment details for the whole population of NSW, the term "medical oncologist" is broadly defined as any practitioner who advises on and oversees chemotherapy for a patient in the survey regardless of their specialist qualifications. It would be expected however, that most clinicians who provided data for this report held an appropriate medical oncology qualification.

Details of chemotherapy treatment were available for 88% of these 920 cases (Table 1).

A comparison using basic demographic information available to the NSW Central Cancer Registry suggests that questionnaires were less likely to be completed for patients in highly-accessible areas than less-accessible areas and patients diagnosed in 2001 than in 2000 (Table 2).

Table 1. Accrual into the survey

		N
New cases of colorectal cancer notified from NSW Central Cancer Registry 1/2/2000 – 31/1/2001		3443
Cases excluded:		66
Practitioner indicated that the patient did not have a diagnosis of colorectal cancer	*36*	
Treatment was administered outside NSW	*9*	
Patient had a previous colorectal cancer notification	*21*	
Eligible cases		3377
Eligible chemotherapy cases		920 (100%)
No response from practitioner		111 (11%)
Chemotherapy questionnaires returned		809 (88%)

Table 2. Characteristics of patients according to whether or not a chemotherapy questionnaire was completed

	Completed Questionnaire					
	Yes		No		Total	
	n	%	n	%	n	%
Age (years)						
0-59	320	40	32	29	352	38
60-69	269	33	38	34	307	33
70-79	196	24	35	32	231	25
80+	24	3	6	5	30	3
Sex						
Male	478	59	70	63	548	60
Female	331	41	41	37	372	40
*ARIA category						
Highly accessible	662	82	98	88	760	83
Accessible	131	16	12	11	143	16
Moderately accessible to very remote	16	2	1	1	17	2
Year of diagnosis						
2001	22	3	10	9	32	3
2000	772	95	99	89	871	95
1999	15	2	2	2	17	2
Total patients	809	89	111	11	920	100

** Accessibility/Remoteness Index of Australia*

Characteristics of patients' cancer

Number of primary cancers

Table 3. Number of primary cancers

Number of primary cancers	Patients	
	n	%
1	778	96
2	31	4
Total patients for whom a chemotherapy questionnaire was returned	809	100

For simplicity and clarity of presentation in this report, all subsequent analyses are based on patients who had only one cancer (n=778). That is, patients with multiple synchronous primary cancers were excluded from the analyses.

Cancer site

Unless stated otherwise, the convention in this report is for the rectosigmoid to be classified as part of the rectum.

Approximately 60% of cancers occurred in the colon, of which the right and left colon accounted for nearly equal proportions (Table 4).

In keeping with the current epidemiological literature on this disease, Table 5 shows a relatively even distribution of colon cancers in men and women and a predominance of rectal cancers in men.

Table 4. Distribution of colorectal cancers

Cancer Site	Total	
	n	%
Right colon	195	25
Caecum	102	13
Ascending colon	79	10
Hepatic flexure	14	2
Transverse colon	48	6
Left colon	226	29
Splenic flexure	27	3
Descending colon	29	4
Sigmoid colon	170	22
Rectosigmoid	71	9
Rectum	238	31
Upper third	57	7
Middle third	97	12
Lower third	84	11
Total patients	778	100

Table 5. Distribution of cancer site by patients' sex and age

	Cancer Site						
	Right colon	Transverse colon	Left colon	Recto-sigmoid	Rectum	Total	
	n=195	n=48	n=226	n=71	n=238		
	%	%	%	%	%	n	%
Sex							
Male	53	50	56	58	70	462	59
Female	47	50	44	42	30	316	41
Age (years)							
0-59	32	42	41	39	45	308	40
60-69	36	33	34	39	29	261	34
70-79	27	23	22	18	24	185	24
80+	5	2	3	3	2	24	3
Total (%)	25	6	29	9	31	778	100

Extent of cancer

For simplicity, we have presented cancer "stage" in terms of the extent of the cancer at diagnosis rather than in categories of any one of the staging schemes (see Appendix 3). The question used to elicit disease extent requested the respondent to "use the most accurate clinical or pathological staging information available". For ease of reference we refer to "extent of cancer" as "stage" hereafter.

There was little difference between the stage distributions of colon cancers and rectal cancers seen by medical oncologists. Approximately half of patients presented with cancers spread to regional nodes (Table 6). Stage was little different between men and women and appeared unrelated to age (Table 7).

Table 6. Distribution of cancer site by cancer stage

	Cancer Stage						
	Submucosa / muscularis	Beyond bowel wall	Regional nodes	Distant metastases	Missing/ unknown	Total	
	n=18	n=107	n=411	n=207	n=35		
	%	%	%	%	%	n	%
Cancer site							
Right colon	1*	17	54	27	1	195	25
Transverse colon	0	15	46	38	2	48	6
Left colon	2	12	54	32	0	226	29
Rectosigmoid	1	7	63	27	1	71	9
Rectum	5	14	50	19	13	238	31
Total (%)	2	14	53	27	5	778	100

** Percentages in this table are row percentages*

Table 7. Distribution of cancer stage by sex, age and remoteness of residence

	Cancer Stage						
	Submucosa / muscularis	Beyond bowel wall	Regional nodes	Distant metastases	Missing/ unknown	Total	
	n=18 %	n=107 %	n=411 %	n=207 %	n=35 %	n	%
Sex							
Male	3*	15	51	26	6	462	59
Female	2	12	56	28	2	316	41
Age (years)							
0-59	3	14	50	28	5	308	40
60-69	2	16	54	25	4	261	34
70-79	3	11	55	25	5	185	24
80+	0	4	63	29	4	24	3
†ARIA category							
Highly accessible	2	14	52	29	4	635	82
Accessible	2	13	62	16	6	127	16
Moderately accessible to very remote	6	19	31	19	25	16	2
Total (%)	2	14	53	27	5	778	100

** Percentages in this table are row percentages*

*†Accessibility/Remoteness Index of Australia defines **five categories** of remoteness based on road distance to service centers.*
The five categories are:
*1. **Highly accessible** (ARIA score 0-1.84) – relatively unrestricted accessibility to a wide range of goods and services and opportunities for social interaction.*
*2. **Accessible** (ARIA score >1.84-3.51) – some restrictions to accessibility of some goods, services and opportunities for social interaction.*
*3. **Moderately accessible** (ARIA score >3.51-5.80) – significantly restricted accessibility of goods, services and opportunities for social interaction.*
*4. **Remote** (ARIA score >5.80-9.08) – very restricted accessibility of goods, services and opportunities for social interaction.*
*5. **Very remote** (ARIA score >9.08-12) – very little accessibility of goods, services and opportunities for social interaction.*
(http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pubs-hfsocc-ocpanew14a.htm/$FILE/ocpanew14.pdf)

Caseloads of surveyed medical oncologists

Almost half (41%) of the patients in this survey were managed by a small proportion (16%) of medical oncologists who were considered to have a high colorectal cancer caseload, ie greater than 30 cases per annum. Slightly over half of the medical oncologists in the survey treated fewer than 15 cases during the 12-month survey period (Table 8).

Patients were more likely to be treated by a higher caseload medical oncologist if they lived in an area with high accessibility to services and were treated in a principal referral hospital (Table 9). The surgical treatment report indicated that a higher proportion of rectal cancer patients were treated by surgeons with higher caseloads (Table 9 of surgical report[1]); this was not so for treatment by medical oncologists.

Patients who lived within the boundaries of a metropolitan or other urban Area Health Service were more likely to receive their chemotherapy care from a practitioner with a higher caseload, compared to patients residing elsewhere (Table 10).

Table 8. Distribution of patients and medical oncologists by medical oncologists' caseload

Medical oncologist caseload*	Patients		Medical oncologists	
	n	%	n	%
<15	153	20	29	56
15-20	141	18	8	15
21-30	164	21	7	13
31-40	206	26	6	12
>40	114	15	2	4
Total	778	100	52	100

** Number of patients' medical oncologist had in the survey*

Table 9. Factors associated with medical oncologists' caseload

	Medical oncologist caseload						
	<15	15-20	21-30	31-40	>40	Total	
	n=153	n=141	n=164	n=206	n=114		
	%	%	%	%	%	n	%
*ARIA category							
Highly accessible	79	82	66	87	96	635	82
Accessible	17	18	32	10	2	127	16
Moderately accessible to very remote	4	1	2	2	2	16	2
Hospital type							
Principal referral	58	36	26	53	85	390	50
Other public	18	39	41	18	1	187	24
Private	23	24	33	29	8	191	25
Unknown	1	1	0	0	6	10	1
Cancer site							
Colon	59	62	59	63	56	469	60
Rectum	41	38	41	37	44	309	40
Cancer stage							
Submucosa/muscularis	3	1	4	1	3	18	2
Beyond bowel wall	18	14	10	18	6	107	14
Regional nodes	44	58	60	52	49	411	53
Distant metastases	29	24	21	26	36	207	27
Missing or unknown	7	2	5	3	6	35	5
Total (%)	18	22	18	22	20	778	100

** Accessibility/Remoteness Index of Australia*

Table 10. Distribution of medical oncologists' caseload by Area Health Service of patients' residence

*Area Health Service	Medical oncologists' caseload						
	<15	15-20	21-30	31-40	>40	Total	
	n=153	n=141	n=164	n=206	n=114		
	%	%	%	%	%	n	%
Metropolitan	78	48	50	81	53	497	64
South Eastern Sydney	29	7	10	31	18	154	20
Central Sydney	7	13	0	1	35	71	9
South Western Sydney	14	0	0	15	0	52	7
Western Sydney	7	12	0	15	0	59	8
Wentworth	5	0	12	1	0	30	4
Northern Sydney	16	16	28	19	0	131	16
Other urban	5	28	26	16	45	172	22
Central Coast	5	13	13	0	0	48	6
Hunter	0	14	12	16	0	73	9
Illawarra	0	0	0	0	45	51	7
Rural	16	23	24	3	0	103	13
Far West	2	0	0	0	0	3	<1
Greater Murray	5	11	0	0	0	24	3
Macquarie	1	0	0	0	0	2	<1
Mid North Coast	0	6	14	0	0	32	4
Mid Western	1	5	7	0	0	19	2
New England	0	0	0	3	0	6	1
Northern Rivers	7	0	0	0	0	10	1
Southern	0	1	4	0	0	7	1
Unknown	1	1	0	0	3	6	1
Total (%)	20	18	21	26	15	778	100

** These area health services refer to the pre-2005 boundaries, the new amalgamated Area Health Services include:*

Metropolitan: *Northern Sydney/Central Coast (Northern Sydney and Central Coast), South Eastern Sydney/Illawarra (South Eastern Sydney and Illawarra), Sydney South West (Central Sydney and South Western Sydney), Sydney West (Western Sydney and Wentworth)*

Rural: *Greater Southern (Greater Murray and Southern), Greater Western (Far West, Macquarie and Mid Western), Hunter/New England (Hunter and New England), North Coast (Northern Rivers and Mid North Coast)*

Characteristics of treating institutions

For estimation of hospital caseload, the treating institution was defined as the hospital that notified the NSW Central Cancer Registry or that indicated by the practitioner, in relation to chemotherapy treatment. The NSW Health's Peer Group system (Appendix 4) was used to identify the hospitals to be designated as principal referral centres.

Higher caseload hospitals were more likely to be situated in metropolitan Area Health Services. They were also more likely to be a principal referral hospital (Table 11).

Patients residing in highly-accessible areas were more likely to be treated in a metropolitan or other urban hospital. They were also more likely to be treated in a principal referral hospital (Table 12). Patients living in accessible areas were least likely to be treated in a principal referral hospital and most likely to be treated in a rural hospital.

Table 11. Types of treating institutions and hospital colorectal cancer chemotherapy caseload

	Hospital caseload						
	<15	15-25	26-35	>35	Unknown	Total	
	n=184	n=182	n=176	n=230	n=6		
	%	%	%	%	%	n	%
Hospital location							
Metropolitan	47	79	66	65	0	497	64
Other urban	10	8	34	35	0	172	22
Rural	43	13	1	0	0	103	13
Unknown	0	0	0	0	100	6	1
Hospital type							
Principal referral	20	29	68	80	0	390	50
Other public	55	21	1	20	0	187	24
Private	23	51	32	0	0	191	25
Unknown	2	0	0	0	100	10	1
Cancer site							
Colon	65	60	61	57	33	469	60
Rectum	35	40	39	43	67	309	40
Cancer stage							
Submucosa/muscularis	1	3	1	4	0	18	2
Beyond bowel wall	13	12	13	17	17	107	14
Regional nodes	61	52	47	52	50	411	53
Distant metastases	22	30	34	22	33	207	27
Missing or unknown	3	3	6	6	0	35	5
Total (%)	24	23	23	30	1	778	100

Table 12. Treating hospital in relation to patients' place of residence

	*ARIA category of patient's residence					
	Highly accessible	Accessible	Moderately accessible	Remote/ Very remote	Total	
	n=635 %	n=127 %	n=10 %	n=6 %	n	%
Hospital location						
Metropolitan	70	28	80	50	497	64
Other urban	24	16	0	0	172	22
Rural	4	56	10	50	103	13
Unknown	1	1	10	0	6	1
Hospital type						
Principal referral	55	26	70	50	390	50
Other public	16	66	10	50	187	24
Private	29	7	10	0	191	25
Unknown	1	1	10	0	10	1
Total (%)	82	16	1	1	778	100

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Diagnostic investigations and surgical management

These aspects of colorectal cancer management were recorded in detail in the surgical questionnaire since surgeons generally are responsible for them. The details are available in the surgical report.[1]

The chemotherapy questionnaire however requested information as to whether the patient had surgery and the type of surgery in broad terms (Table 13).

Table 13. Surgical treatment by site of cancer and stage

	Surgical Procedure						
	No surgery	Colectomy	Anterior resection	AP resection	Other	Total	
	n=26 %	n=349 %	n=246 %	n=71 %	n=86 %	n	%
Cancer site							
Colon	2*	73	15	<1	9	469	60
Rectum	5	3	57	23	13	309	40
Total (%)	3	45	32	9	11	778	100

** Percentages in this table are row percentages*

Overview of use of chemotherapy

Adjuvant postoperative treatment for colon and rectal cancer was the most common reason for patients receiving chemotherapy. Treatment was given to control metastatic disease for 22% of patients (Table 14).

Table 14. Reasons for receiving chemotherapy

Indications for chemotherapy	Total	
	n	%
Adjuvant postoperative treatment for colon cancer	348	45
Adjuvant postoperative treatment for rectal cancer	177	23
Preoperative treatment for *locally advanced, inoperable* rectal cancer	30	4
Preoperative treatment for *operable* rectal cancer	54	7
Treatment of *asymptomatic* metastatic disease	79	10
Palliation of symptoms from metastases	90	12
Total	778	100

Adjuvant chemotherapy for colon cancer

Guideline
"People with resected node-positive colon cancer should be offered adjuvant therapy." (Level I evidence)

"The value of adjuvant therapy in Dukes B (stage II) colon cancer has not been demonstrated uniformly. Adjuvant therapy in this group is not recommended except for patients with 'poor prognosis' stage II disease who, after discussion, wish to have treatment or entry into an appropriate clinical trial, which is recommended." (Level II evidence)

Chemotherapy questionnaires were only sent out if a patient was identified as having received this treatment. As referrals for adjuvant chemotherapy for colon cancer are generally made by the patients' surgeons, the surgical questionnaire surveyed their referral patterns. An analysis of the referral patterns can be found in the surgical report (Tables 45-49).[1] Briefly, it was found that approximately 40% of patients with colon cancer who had regional lymph node involvement did not receive adjuvant chemotherapy. In about half of these cases, the patient was not referred to a medical oncologist because the attending surgeon stated that he or she felt that this was "not indicated". Of 469 patients with colon cancer who received chemotherapy, 348 patients received adjuvant chemotherapy.

The denominator for this section will therefore be 348 patients.

Table 15. Distribution of cancer site by cancer stage for patients receiving adjuvant therapy for colon cancer

	Cancer Stage						
	Submucosa / muscularis	Beyond bowel wall	Regional nodes	Distant metastases	Missing/ unknown	Total	
	n=6	n=69	n=248	n=22	n=3		
Cancer site	%	%	%	%	%	n	%
Right colon	1*	22	69	6	1	152	44
Transverse colon	0	21	67	9	3	33	9
Left colon	3	17	74	6	0	163	47
Total (%)	2	20	71	6	1	348	100

** Percentages in this table are row percentages*

Adjuvant chemotherapy was given in accordance with the guidelines in 71% of patients who received it. Patients with Dukes B colon cancer were 22% of those who received it; this proportion is probably too high to be explained by clinical trial use. Since 70% of all Dukes D cases in the survey were referred for chemotherapy it is possible that some of the small group of patients who had distant metastases at diagnosis and chemotherapy were incorrectly stated as having *adjuvant* therapy.

Forty-four percent of patients received chemotherapy more than six weeks after surgery. The presence of surgical complications, age, sex and geographic accessibility do not seem to account for delay in treatment (Table 16).

Table 16. Time interval between surgery and chemotherapy for colon cancer

	Time interval (weeks)					
	<3	3-6	>6	unknown	Total	
	n=25	n=161	n=153	n=9		
	%	%	%	%	n	%
Major postoperative complication						
Yes	7*	47	44	3	299	86
No	10	44	44	2	48	14
Unknown	0	0	100	0	1	<1
Age (years)						
0-59	7	42	49	2	125	36
60-69	9	47	42	2	125	36
70-79	6	51	39	4	84	24
80+	0	50	50	0	14	4
Sex						
Males	10	48	41	2	189	54
Females	4	45	48	3	159	46
#ARIA category						
Highly accessible	7	44	46	3	287	83
Accessible	9	53	37	2	57	16
Moderately accessible to very remote	0	100	0	0	4	1
Total (%)	7	46	44	3	348	100

** Percentages in this table are row percentages*
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Guideline
"5-FU plus low-dose leucovorin for six months is the preferred option. Other adjuvant therapy regimens with similar reductions in the rate of relapse and mortality (30–40%) include:
5-FU plus low-dose leucovorin ± levamisole for six months; and
5-FU plus levamisole for one year." (Level II evidence)

Most patients received 5-FU plus leucovorin with intended duration of six months. Only 9% had high-dose leucovorin.

Table 17. Type and duration of adjuvant chemotherapy for colon cancer

Drugs used	Intended months of duration					
	1-5	6	>= 7	Unknown	Total	
	n=14	n=328	n=1	n=5		
	%	%	%	%	n	%
5-FU based	4*	94	<1	1	341	98
Modulation of 5-FU:						
None	25	75	0	0	8	2
Low-dose IV leucovorin (<50mg/m²/dose)	4	95	<1	1	287	82
High-dose IV leucovorin (≥50mg/m²/dose)	3	97	0	0	33	9
Oral leucovorin	0	100	0	0	5	1
Levamisole	0	0	0	0	0	0
Other drug	0	88	0	12	8	2
Non 5-FU based	0	86	0	14	7	2
Total (%)	4	94	<1	1	348	100

**Percentages in this table are row percentages*

Table 18. Scheduling of 5-FU adjuvant chemotherapy for colon cancer

Scheduling	n	%
Mayo Clinic (daily x5, repeated 4th weekly)	186	55
Roswell Park (once a week)	123	36
Infusion during radiotherapy	1	<1
Infusion only	5	1
Other	26	8
Total patients receiving 5-FU	341	100

Adjuvant chemotherapy for rectal cancer

Guideline
"Postoperative 5-FU based chemotherapy and radiotherapy (combined modality therapy) is recommended for patients with high-risk rectal cancer." (Level II evidence)

As in the previous section, referral patterns for adjuvant chemotherapy in rectal cancer were assessed in the surgical questionnaire, and further details can be found in the surgical report.[1] Briefly, it was found that about half of patients with high-risk rectal cancer did not receive chemotherapy. In 37% of these cases, the surgeon stated that this treatment was "not indicated". Thirty-three percent of patients with high-risk rectal cancer received radiotherapy. In 57% of these cases, the surgeon stated that this treatment was not indicated. Only a small proportion of high-risk rectal cancer patients had postoperative combined modality therapy; on the other hand a reasonable proportion of these cases received preoperative radiotherapy in lieu.
Of 309 patients with rectal cancer who received chemotherapy, 231 patients had adjuvant chemotherapy.

The denominator for this section will therefore be 231 patients.

Sixty-seven percent of patients who received adjuvant chemotherapy for rectal cancer had disease that had spread to regional lymph nodes but not more distantly.

Thirty-nine percent of patients received adjuvant chemotherapy only (Table 19); 52% received chemotherapy with concurrent radiotherapy and 9% with non-concurrent radiotherapy (Table 20). Chemotherapy was given postoperatively in 83% of patients and with concurrent postoperative radiotherapy in 36% (Table 20).

Table 19. Chemotherapy ± radiotherapy given[§] by cancer stage

	Cancer Stage						
	Submucosa / muscularis	Beyond bowel wall	Regional nodes	Distant metastases	Missing/ unknown	Total	
	n=11	n=28	n=155	n=12	n=25		
	%	%	%	%	%	n	%
Age (years)							
0-59	5*	11	66	7	11	95	41
60-69	4	15	67	4	10	79	34
70-79	6	9	74	0	11	53	23
80+	0	25	0	50	25	4	2
Sex							
Male	4	14	64	5	14	154	67
Female	6	8	74	6	5	77	33
[#]ARIA category							
Highly accessible	4	12	68	7	10	182	79
Accessible	7	14	69	0	10	42	18
Moderately accessible to very remote	14	0	43	10	43	7	3
Adjuvant therapy							
Chemotherapy only	2	7	84	4	2	90	39
Combined modality therapy	6	16	56	6	16	141	61
Total (%)	5	12	67	5	11	231	100

** Percentages in this table are row percentages*

[§] Covers both pre and postoperative treatments

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Table 20. Timing of adjuvant chemotherapy and radiotherapy given to patients with rectal cancer

	n	%
Chemotherapy only	90	39
Preoperative	1	1
Postoperative	89	38
Combined modality therapy	141	61
Concurrent radiotherapy use	*120*	*52*
Preoperative	37	16
Postoperative	68	29
Pre and postoperative	15	7
Non concurrent radiotherapy use	*21*	*9*
Postoperative chemotherapy plus preoperative radiotherapy	14	6
Postoperative chemotherapy plus postoperative radiotherapy (not concurrently)	7	3
Total patients with adjuvant chemotherapy for rectal cancer	231	100

Guideline

"When chemotherapy is given postoperatively in combination with radiotherapy, protracted venous infusion of 5-FU chemotherapy may offer further benefits in survival when compared to bolus 5-FU therapy. It is the recommended way of delivering combined modality therapy." (Level II evidence)

Fifty-nine percent of patients having concurrent 5-FU chemotherapy and radiotherapy for rectal cancer received their 5-FU by continuous infusion during their radiotherapy treatment sessions.

Chemotherapy complications

The reported rate of complications requiring admission was low, with 86% of patients not reported as experiencing any complications of sufficient severity to require hospital admission. Enteritis or diarrhoea was the most common complication with 8% of patients affected; this figure includes patients who had multiple complications (Table 21).

Table 21. Complications of chemotherapy that required admission, by site of primary cancer

Complication	Cancer site			
	Colon	Rectum	Total	
	n=469 %	n=309 %	n	%
No complication	86	86	671	86
Enteritis/diarrhoea alone	4	4	31	4
Enteritis/diarrhoea plus stomatitis	1	2	9	1
Enteritis/diarrhoea plus febrile neutropenia	2	1	10	1
Enteritis/diarrhoea plus stomatitis and febrile neutropenia	2	2	12	2
Stomatitis	<1	0	2	<1
Stomatitis plus febrile neutropenia	<1	0	1	<1
Febrile neutropenia	2	1	10	1
#Other	4	5	29	4
Unknown or missing	<1	<1	3	<1
Total (%)	60	40	778	100

 # 29 'other' complications include: 11 thromboembolic complication, 5 abdominal symptom, 5 infective complication, 3 cardiac complication, 1 anxiety, 1 chest pain, 1 confusion and fever, 1 depression, 1 dysaesthesia.

Management of metastatic colorectal cancer

Guideline
"First-line 5-FU-based chemotherapy prolongs life when compared to best supportive care and should be offered to patients with advanced colorectal cancer." (Level II evidence)

"5-FU plus leucovorin, 5-FU plus methotrexate, and continuous infusion 5-FU are all associated with an improvement in response rate over 5-FU alone. Survival advantages in the palliative setting may exist, but are small with no clear quality-of-life benefits over 5-FU alone." (Level I evidence)

The surgical questionnaire data indicated that 52% of patients with Stage IV colon cancer and 58% of patients with Stage IV rectal cancer received chemotherapy (Table 48 and Table 54 of surgical report [1]).

Most patients (92%) who had chemotherapy for metastatic colorectal cancer received 5-FU based treatment (Table 22). Seventy-four percent of patients receiving 5-FU also received leucovorin, either orally or intravenously.

Table 22. Chemotherapy type given to patients with metastatic colorectal cancer

Drugs used	n	%
5-FU based	155	92
No modulation	29	17
Low-dose IV leucovorin (<50mg/m^2/dose)	94	56
High-dose IV leucovorin (≥50mg/m^2/dose)	18	11
Oral leucovorin	11	7
Methotrexate	0	0
Other	3	2
Non 5-FU based	14	8
Irinotecan	1	1
Raltitrexed	5	3
Oxaliplatin	1	1
other	7	4
Total patients with metastatic colorectal cancer	169	100

Bolus scheduling of 5-FU was more common (85%) than infusion scheduling (15%) (Table 23).

Table 23. Scheduling of 5-FU for patients with metastatic colorectal cancer

Scheduling	n	%
Bolus	132	85
Infusion:	23	15
For rectal cancer	9	6
For colon cancer, without 5-FU modulation	12	8
For colon cancer, with 5-FU modulation	2	1
Total patients receiving 5-FU	155	100

Hepatic arterial infusion

Guideline
"Hepatic arterial infusion (HAI) has shown survival benefit compared with best supportive care." (Level II evidence)

"HAI shows higher response rates but little evidence of survival advantage compared with systemic chemotherapy." (Level I evidence)

"HAI and intravenous chemotherapy should be regarded as acceptable alternatives." (Level I evidence)

The surgical management of isolated liver metastases was dealt with in the surgical report.[1] Fifty-six percent of the 456 patients with Stage IV cancer who underwent surgical treatment had isolated liver metastases; of these 14 (5%) had liver resection and 12 (5%) had a hepatic arterial infusion catheter inserted at the time of initial surgical management.

The chemotherapy questionnaire identified 22 patients who received chemotherapy by hepatic arterial infusion; thus it appears that at least 10 patients had a hepatic arterial infusion catheter inserted following their initial surgery. Half the patients given chemotherapy by hepatic arterial infusion received 5-FU in combination with intravenous leucovorin (Table 24).

Table 24. Choice of chemotherapy for hepatic arterial infusion

Drugs used	n	%
5-FU only	5	23
5-FU plus IV leucovorin	11	50
Non 5-FU based	6	27
Total receiving hepatic arterial infusional chemotherapy	22	100

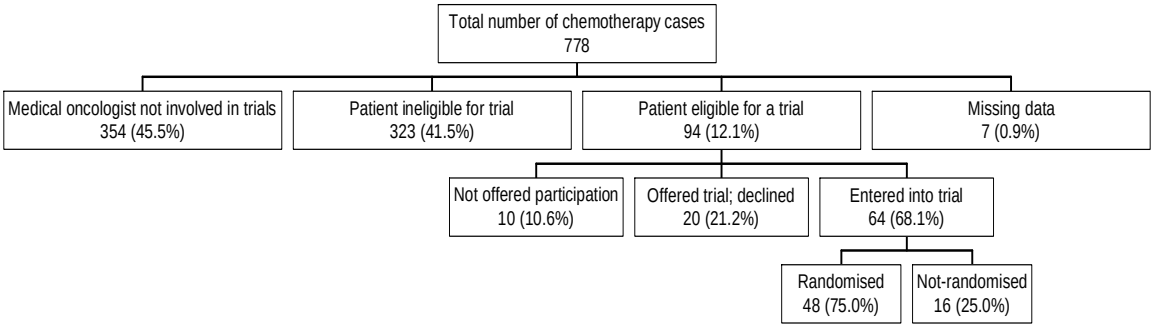
Participation in clinical trials

Guideline
"Doctors should encourage patients with colorectal cancer to consider participating in appropriate clinical trials for which they are eligible." (Expert opinion)

Medical oncologists attending nearly half the patients indicated that they "were not involved in any clinical trials".

Medical oncologists considered 12% of the patients to be eligible for a clinical trial. Of this group, 68% were recorded as having been entered into a clinical trial. Three-quarters of those entered were recorded as having been randomised. Thus the actual proportion of patients participating in a clinical trial was 8%.

Figure 1. Participation of chemotherapy patients in clinical trials



Follow-up intentions

Guideline
"Follow up of patients after curative resection for colorectal cancer is recommended as it allows practitioners to monitor patient outcomes arising from their treatment, and it is consistent with patients' desires." (Expert opinion)

"All patients who have undergone surgery for colorectal cancer should have specialist follow up in conjunction with the patient's general practitioner." (Expert opinion)

Medical oncologists intended to follow up 68% of patients they had treated with chemotherapy. The intention to follow up a patient was greatest when the cancer had spread to regional lymph nodes or distant sites (Table 25).

Table 25. Medical oncologists follow-up intentions for patients treated with chemotherapy by characteristics of patients and cancer *

Patient characteristics	Follow-up intentions				
	Intended	Not intended	Unknown or missing	Total	
	n=496	n=167	n=62		
	%	%	%	n	%
Age (years)					
0-59	68[†]	23	9	289	40
60-69	72	23	6	246	34
70-79	65	25	10	168	23
80+	68	14	18	22	3
[#]ARIA category					
Highly accessible	69	22	9	592	82
Accessible	67	26	8	117	16
Moderately accessible to very remote	56	44	0	16	2
Cancer stage					
Submucosa/muscularis	44	33	22	18	2
Beyond bowel wall	56	39	5	104	14
Regional nodes	72	20	8	404	56
Distant metastases	77	13	11	168	23
Missing or unknown	32	61	6	31	4
Surgery or radiotherapy given					
Surgery only	73	18	9	542	75
Radiotherapy only	75	13	13	8	1
Surgery and radiotherapy	54	41	5	168	23
Neither	86	0	14	7	1
Total (%)	68	23	9	725	100

** Excludes 53 cases that are deceased or their vital status is unknown*
[†] Percentages in this table are row percentages
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Further analyses proposed

The data collected for this survey are intended for further analysis and publications. These include the following:

Reports from other data collected in this survey

A similar report will be released on radiotherapy treatment for colorectal cancer, once data analysis has been finalised.

Follow-up data on patient outcomes were collected in 2003 and will be covered in a separate report.

Further analysis and dissemination of data collected on surgical management

Further analysis will be undertaken to identify demographic variables pertinent to patients, practitioners and hospitals that are associated with concordance of colorectal cancer management with the NHMRC guideline recommendations. These data will be submitted for consideration of publication in major peer-reviewed medical journals.

Economic analysis will be undertaken to estimate the direct health costs incurred in NSW for the management of colorectal cancer.

In addition, third parties may request the data collected in suitably de-identified form for further analysis. Proposals should be made in writing and are subject to the approval of the survey's Expert Advisory Group and any necessary ethical clearances. Such proposals can be discussed beforehand by contacting either:

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Appendices

Appendix 1 Chemotherapy Questionnaire

Form No: NC

A. Details of tumour

1. Site(s) of primary tumour:
   - 1☐ caecum
   - 2☐ ascending colon
   - 3☐ hepatic flexure
   - 4☐ transverse colon
   - 5☐ splenic flexure
   - 6☐ descending colon
   - 7☐ sigmoid colon
   - 8☐ rectosigmoid
   - 9☐ rectum, upper third
   - 10☐ rectum, middle third
   - 11☐ rectum, lower third

2. Number of primary tumours: _____

3. (a) Local tumour stage *(use the most accurate clinical or pathological staging information available; for >1 primary, select most advanced)*:
   - a1☐ unknown
   - a2☐ carcinoma *in situ*
   - a3☐ submucosal involvement
   - a4☐ involvement of muscularis
   - a5☐ subserosa (or perirectal tissues)
   - a6☐ serosal involvement
   - a7☐ adjacent organ invasion

   (b) Spread to lymph nodes (any combination):
   - b1☐ unknown
   - b2☐ not involved
   - b3☐ epi-, para-, retro-colic or mesenteric
   - b4☐ apical
   - b5☐ distant: _____ (name chain)

   (c) Sites of distant spread (any combination):
   - c1☐ none known
   - c2☐ non-adjacent peritoneum
   - c3☐ liver
   - c4☐ lung
   - c5☐ other(s): _____

B. Chemotherapy details

4. Did the patient receive chemotherapy? *(*tick one*)*

   Yes
   - 1☐ before surgery
   - 2☐ after surgery
   - 3☐ before and after surgery
   - 4☐ patient did not have surgery

   → *go to next question (5)*

   No
   - 5☐ offered but declined
   - 6☐ not indicated
   - 7☐ other reason: _____

   → *skip to question 9*

5. Indication for chemotherapy (tick one):
   - 1☐ adjuvant post-operative treatment (no pre-operative chemotherapy)
   - 2☐ pre-operative treatment for *locally advanced, inoperable* rectal cancer
   - 3☐ pre-operative treatment for *operable* rectal cancer
   - 4☐ treatment of *asymptomatic* metastatic disease
   - 5☐ palliation of symptoms from metastases

6. Planned chemo duration: _____months (a)

   Treatment start date: ___/____/ ___(b)

   Has treatment finished? c1☐ no c2☐ yes

   If yes, date finished:____/____/ ___(d)

7. Details of treatment regimen on which the patient was *first started*:

   A. Route (any combination)
   - a1☐ oral
   - a2☐ intravenous
   - a3☐ intrahepatic

   B. Drugs (any combination)
   - b1☐ 5-Fluorouracil
   - b2☐ oral leucovorin
   - b3☐ IV Leucovorin, < 50mg/m^2/day
   - b4☐ IV Leucovorin, ≥ 50mg/m^2/day
   - b5☐ levamisole
   - b6☐ methotrexate
   - b7☐ raltitrexed (Tomudex)
   - b8☐ irinotecan (CPT-11, Campostar)
   - b9☐ oxaliplatin
   - b10☐ other(s): _____

   C. 5FU scheduling (if applicable)
   - c1☐ Mayo regimen/equivalent (bolus, 5 consecutive days, 4th weekly)
   - c2☐ Roswell Park regimen or equivalent (single weekly bolus)
   - c3☐ infusion during radiotherapy
   - c4☐ infusion only
   - c5☐ other: _____

Page 1

Form No: NC

8. Did the patient *require hospitalisation* for any treatment complications?
   - a1☐ no
   - a2☐ Yes (any combination):
     - b1☐ enteritis/diarrhoea
     - b2☐ stomatitis
     - b3☐ febrile neutropenia
     - b4☐ other: _____

9. Is this patient eligible for any clinical trial you may be involved in?
   - a1☐ I am not involved in any trials
   - a2☐ patient was not eligible
   - a3☐ patient was eligible for a trial →
     - Was the patient entered?
     - b1☐ Yes
     - b2☐ Offered but declined
     - b3☐ Not offered
     - Study type:
     - c1☐ randomised
     - c2☐ non-randomised

10. Did the patient receive radiotherapy? *(*tick one*)*
    - Yes 1☐ with chemotherapy
    - 2☐ not with chemotherapy, pre-operatively
    - 3☐ not with chemotherapy, post-operatively
    - No 4☐

11. Did the patient undergo surgery?
    - a1☐ No
    - a2☐ Yes: → Date: _____ / ____ / ___
      - Operation performed:
      - b1☐ colectomy
      - b2☐ anterior resection
      - b3☐ abdomino-perineal resection
      - b4☐ other: _____

C. Follow-up

12. Are you aware of this patient's tumour recurring or progressing?
    - a1☐ no → *go to next question (13)*
    - a2☐ yes → Date of relapse or progression: ____/ ___ / ____

(continued next column)

Sites involved (any combination):
- b1☐ primary site
- b2☐ liver
- b3☐ lung
- b4☐ other: _____

Evidence available (any combination):
- c1☐ pathology
- c2☐ radiology
- c3☐ endoscopy
- c4☐ clinical
- c5☐ rise in serum CEA

Has the patient been referred to a palliative care service?
- d1☐ yes
- d2☐ offered but patient declined
- d3☐ not indicated
- d4☐ this service is not available

13. As far as you know, is the patient alive?
    - a1☐ **No** →Date of death: __ / ___/____
      - Cause of death: (tick one)
      - b1☐ colorectal cancer
      - b2☐ treatment complication (state:_____)
      - b3☐ other cause: _____
      - b4☐ unknown
    - a2☐ **Yes** →Date last known to be alive: ___/ ___ / ____
      - Will the patient be returning to see you for follow-up visits?
      - c1☐ no
      - c2☐ yes → we may wish to send you a brief follow-up questionnaire in 12 months. If this patient will be followed-up at a different practice address, please give the address:
        _____
        _____

14. We may wish to obtain further details of surgery and radiotherapy. Please provide names and addresses if applicable, for these practitioners:
    Attending surgeon:
    _____
    _____
    Attending radiation oncologist:
    _____
    _____

THANK YOU FOR YOUR COOPERATION **Page** 2

Appendix 2 Membership of the Expert Advisory Group

- Dr Stephen Ackland, Department of Medical Oncology, Newcastle Mater Hospital.
- Professor Bruce Armstrong*, Head, School of Public Health and Medical Foundation Fellow, University of Sydney.
- Associate Professor Pierre Chapuis, Department of Surgery, Concord Hospital.
- Dr Andrew Kneebone, Department of Radiation Oncology, Liverpool Hospital.
- Dr David Leong*, Medical Oncologist, PhD student, Centre for Clinical Epidemiology and Biostatistics, University of Newcastle.
- Associate Professor Dianne O'Connell, Senior Epidemiologist, Cancer Epidemiology Research Unit, Cancer Council NSW.
- Associate Professor Michael Solomon, Department of Surgery, Royal Prince Alfred Hospital.
- Professor Allan Spigelman*, Professor of Surgical Science, Faculty of Health, University of Newcastle; Director, Clinical Governance Unit and Area Cancer Services, Hunter New England Area Health Service.

** Chief investigators*

Appendix 3 Cancer stage assignment using questionnaire responses

For reference, the chemotherapy questionnaire is in Appendix 1.

Questionnaire response			Cancer stage		
Local spread:	**Spread to nodes:**	**Distant spread:**	**ACP Stage**	**Dukes' Stage**	**TNM Stage**
Carcinoma in-situ	Not involved	No distant spread	A0	¢-	0 (T1sN0M0)
Submucosa	Not involved	No distant spread	A	¥A	I (T1N0M0)
Muscularis propria	Not involved	No distant spread	A	A	I (T2N0M0)
Subserosa serosal	Not involved	No distant spread	B	£B	II (T3N0M0)
Adjacent organ(s)	Not involved	No distant spread	B	B	II (T4N0M0)
Any except line of resection	Epi-, para-, retro-colic or mesenteric	No distant spread	C	C	III (Any T, N1M0)
Any except line of resection	Apical node(s)	No distant spread	C	C	III (Any T, N2M0)
Line of resection	Yes or No	No distant spread	D	Not* defined	IV (Any T, Any N, M0)
Any	Yes or No	Non-adjacent peritoneum Liver Lung Other	D	Not* defined	IV (Any T, Any N, M1)

¢ This would be classified as "A" under the Astler & Coller modification of Dukes' staging

¥ This would be classified as "B1" under the Astler & Coller modification of Dukes' staging

£ This would be classified as "B2" under the Astler & Coller modification of Dukes' staging

* Not defined in classical Duke's classification

Appendix 4 Classification of hospitals

Area Health Services

The table below lists NSW's Area Health Services (AHSs), which are further classified into Metropolitan, Other urban or Rural according to the hospital's AHS attachment.

Classification of hospitals by NSW AHS attachment

Area Health Service	Classification
Central Sydney	Metropolitan
South Eastern Sydney	Metropolitan
South Western Sydney	Metropolitan
Western Sydney	Metropolitan
Wentworth	Metropolitan
Northern Sydney	Metropolitan
Central Coast	Other urban
Hunter	Other urban*
Illawarra	Other urban*
Far West	Rural
Greater Murray	Rural
Macquarie	Rural
Mid North Coast	Rural
Mid Western	Rural
New England	Rural
Northern Rivers	Rural
Southern	Rural

** The exceptions are for Cessnock, Maitland, Muswellbrook and Shoalhaven district hospitals, which are classified as rural.*

Principal referral hospitals

NSW Health's Peer Group system was used to classify hospitals as principal referral centres. Further details are available on the NSW Health website on http://www.health.nsw.gov.au/pubs/h/yb9798/hospgrps.html. Such hospitals include:

- Concord Hospital
- Gosford District Hospital
- Illawarra Regional Hospital
- John Hunter Hospital
- Liverpool Hospital
- Nepean Hospital
- Prince of Wales Hospital
- Prince Henry Hospital
- Royal North Shore Hospital
- Royal Prince Alfred Hospital
- St George Hospital
- St Vincent's Hospital (Darlinghurst)
- Westmead Hospital

Appendix 5 References

1. Armstrong K, O'Connell DL, Leong D, Spigelman AD, Armstrong BK. *The New South Wales Colorectal Cancer Care Survey Part 1-Surgical Management.* The Cancer Council NSW, 2004. http://www.cancercouncil.com.au/editorial.asp?pageid=1021
2. Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR) 2003. *Cancer in Australia 2000*. AIHW cat. no. CAN 18. Canberra: AIHW (Cancer Series no. 23).
3. Gastrointestinal Tumor Study Group: Prolongation of the disease-free interval in surgically treated rectal carcinoma. N Engl J Med 1985; 312:1465-72.
4. Moertel CG, Fleming TR, MacDonald JS et al. Levamisole and Fluorouracil for adjuvant therapy of resected colon carcinoma. N Engl J Med 1990; 332:352-8.
5. National Health and Medical Research Council. *Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer*. Canberra: AGPS, 1999.
6. Lomas J, Anderson K, Dominck-Pierre et al. Do practice guidelines guide practice? N Eng J Med 1989; 321:1306-11.
7. McArdle CS, Hole D. Impact of variability among surgeons on postoperative morbidity and mortality and ultimate survival. BMJ 1991; 302:1501-1505.
8. Phillips RKS, Hittinger R, Blesovsky L et al. Local recurrence following 'curative' surgery for large bowel cancer: I. The overall picture. Br J Surg 1984; 71:12-16.
9. Hermanek P, Wiebelt H, Staimmer D, Riedl S and the German Study Group Colo-Rectal Carcinoma (SGCRC) Prognostic factors of rectum carcinoma - experience of the German Multicentre Study SGCRC. Tumori 1995; 81(Supplement):60-64.
10. NIH Consensus Conference: Adjuvant therapy for patients with colon and rectal cancer. JAMA 1990; 264:1444-1450
11. Burton RC. Surgery and cancer: opinion, evidence and proof. J Surg Oncol 1999; 71:1-3.
12. Spigelman AD, McGrath DR. Clinical Governance Unit 2002: *The National Colorectal Cancer Care Survey. Australian clinical practice in 2000*. National Cancer Control Initiative, Melbourne, 1-124.
13. Tracey E, Supramaniam R. *Cancer in New South Wales. Incidence and Mortality 2000*. Sydney: The Cancer Council NSW, 2002.