Appendix 1

Birmingham and West Midlands Regional Cancer Registry

Cancer Registries are of two kinds: hospital-based, or population-based. The first registers all cases of cancer seen at one hospital or a small group of hospitals; the second aims to record every case of cancer occurring in a defined population.

A1.1 Beginnings

The Birmingham Cancer Registry - although population based since 1957 - can be said to have begun in the form of a hospital-based registry, when a clerical officer was appointed towards the end of 1935 to complete the forms requested by the Radium Commission. This Commission, set up in 1929, had been empowered to purchase and distribute radium, as the best-known and most useful source of radiotherapy, to the major hospitals of the country to aid in the treatment of cancer. It had requested some information concerning the patients treated by radium in order to provide some feedback on the efficacy of the programme. In an attempt to establish the value of radium in relation to other forms of treatment - chiefly surgery - details of patients not treated by radium were also requested. Radiotherapists, as the users of radium, readily complied, but unfortunately surgeons were less ready to do so, as they felt no similar sense of obligation.

The person appointed to undertake the work of data collection in the Birmingham General Hospital and the Queen's Hospital (now the Accident Hospital) was Miss Joan Levi, a woman of great drive and energy, motivated by an over-riding sense of the importance of the work. Many will remember her and the force of her character: the pressure she would bring to bear on individual clinicians to maintain as complete a record as possible. The Registry owes much to her effort, both in the early days and subsequently, for the strength of the foundations she laid and for much of the superstructure put upon them.

The war saw the destruction of most of the records of the Radium Commission when their offices were bombed in 1944. The Registrar General then took over the responsibility of collecting the data from hospitals. Though Miss Levi's diligence led to the inclusion in the files of every case of cancer, treated or not, the registry was what would nowadays be called hospital-based. With the advent of the Health Service in 1948 and the regionalisation of cancer services the collection of similar data on a regional scale became possible, the regions being the units of administration, each based on several millions of population.

A Regional Cancer (Co-ordinating) Committee was set up in this Region, as in others. A small sub-committee of four of its members (the Professors of Medicine, Surgery and Pathology and the Reader in Medical Statistics - Dr. Waterhouse) was formed which recommended setting up a Cancer Registry. It was one of the first to be set up in this country. It centralised the collection of data about cancer patients for the Region and undertook the responsibility of making returns to the Registrar General for the Region as a whole, rather than individually by hospitals. Thus each hospital provided information directly to the Registry, and the Registry to the Registrar General. This is now the pattern throughout the country.

The Director, Dr. Waterhouse, decided that the records should be kept in the original form as submitted to the Registry (together with any subsequent pathology and follow-up reports etc.) and also in coded form on punch cards (and later on computer) to facilitate retrieval of data and analysis. A standard set of forms was devised for the collection of the data, requesting rather more than the basic minimum required by the Registrar General. In addition to the basic identification and social data about the patient and the names of the clinicians and hospitals involved, a full description of the tumour, both macroscopic and microscopic, and of the treatment given is recorded. Follow-up reports are added, together with details of any extension of the growth (recurrences or metastases), the development of fresh primaries, and descriptions of the treatment given. At this time, the International Classification of Diseases chapter for neoplasms was inadequate, so that it became necessary to design a completely new system of hierarchical and contingent codes.

Naturally the Registry was not immediately fully effective or complete. There was no form of compulsion to provide data, nor active encouragement in the form of a fee (as for the notifiable diseases) so the system depended on voluntary agreement, though the mechanics of the system were provided by registration clerks (some specially appointed) in the various hospitals. The year 1960 is generally considered to be the year when close to 95% coverage was achieved, resulting at that time in a total of just over 15,000 new cases. Twenty years later the total of the new registrations was about 22,000 a year, the increase being partly due to the ageing of

the population (whereby more people are now living into the older ages where cancer is more common), and partly to the increased incidence of certain kinds of cancer (chiefly lung, bladder and prostate).

It is not only hospitals which are involved in providing data for the Cancer Registry. Routinely, all pathology laboratories provide copies of pathology reports referring to cancer; coroners and their pathologists supply information on the extent of the disease at autopsy; general practitioners are most helpful in providing information on follow-up, including recurrence or further treatment, and the Registrar General sends copies of all death certificates containing any mention of cancer.

A1.2 Aims

What is the purpose of cancer registration - of collecting and storing a vast amount of information on patients with a single disease (or rather, group of diseases) which number now, in the Birmingham Cancer Registry, close to a half million cases? It began as a record of patients treated in a specific way in order to evaluate that mode of therapy. It is still patient-based (or, more properly, tumour-based, because a patient with two distinct primary cancers has two registrations) and it can be - and is - used for the evaluation of treatment regimens, though in rather more sophisticated ways than before. As a population-based registry, however, it acquires another mode of usefulness, in an epidemiological sense. When it is possible, as now, to discuss and analyse data referring to almost all patients (98%) with cancer in a region of 5.2 million population (the largest in the U.K.), to localise the tumour itself and its degree of spread, as well as the patient's residence, his treatment and his fate, the detailed impact of the disease on a representative community can be very fully described and measured. Furthermore, changes and trends in the interaction between disease and community (which is the subject matter of epidemiology) can be detected and monitored. To some extent this can be done by the Registrar General for the country as a whole from the returns he receives from each regional registry, but his data are necessarily limited by the strength of the weakest link in the chain of registries; some are very poor, and none has the wide range of data that Birmingham has. The passion of legislators to change the boundaries of administrative units and sub-units has affected many internal sub-divisions of the West Midland Region but (fortunately and uniquely in the United Kingdom) has left its outer boundaries unchanged. Thus it is possible to study and compare the changing patterns of cancer in a single sizeable area over a period of about a quarter century.

Internally, appropriate statistical indices can serve to characterize the pattern of cancer, by site, sex, age group, geographical sublocation, etc., with obvious relevance to the provision of adequate services for diagnosis, treatment, follow-up, terminal care, etc. Such statistics, if kept in a uniform fashion over a period of time, will also furnish indications of changes in the impact of the disease, necessitating alterations in the services provided. It is also possible by extrapolation, based on plausible assumptions, to predict the requirements for the future. At the same time, the changes observed in the pattern of disease can be set against other characteristics (for example, occupational, environmental, or geographical) in order to serve the purpose of monitoring the effects of known carcinogenic agents, and of detecting potentially new hazards.

In addition to the information they provide for cancer services, and for the observation of changes in the impact of the disease, the same or similar statistics can be used for teaching, both undergraduate and postgraduate; and for clinical purposes, to evaluate the efficacy of treatment, to compile data on the natural history of the disease, or to assess the role of early diagnosis programmes.

Appendix 2
Standardised Rates

A2.1 Standardised incidence rates

The very steep increase in risk with increasing age, which is characteristic of nearly all cancers makes the number of cases likely to occur in a given "population" (or defined group of people) very sensitive to their composition by age. In consequence, if the population includes a relatively large proportion of the elderly, more cancer cases are likely to be found than in a younger population.

The most convenient summary of the incidence of cancer in a population is expressed by the overall rate - that is, the total number of cancers divided by the total number of people in the population. Thus, if there are 800 cases in a population of 200,000, the rate would be quoted as 4 per 1000, or 400 per 100,000; either form could be used. This defines what is often called the "crude" rate, in contrast to the age specific rates which would be obtained by subdividing both the population and the cases of cancer into age groups (either five year, such as 35-39, etc: or ten-year, such as 30-39, or 35-44) and calculating an incidence rate for each age group. When subdividing also by sex, the numbers of cases in some of the age groups will be rather small, and thus lead to rates which may not be very representative or stable.

It would avoid the problems of dependency on the age structure of a population if we could always use the same one - a "standard population" of known and constant composition. But each individual population encountered in practice, has its own constitution by age. If however the age specific rates are calculated from that given population, and then applied to the standard population, age group by age group, to obtain the number of cases that would be expected to occur in the standard population if it had experienced the rates, at each age group, of the given population, then the total of the

expected cases can be used to provide the analogue of a crude rate in the standard population. This rate is then known as the "standardised rate" for the given population. The nature of the standard population needs to be specified also. In contemporary usage, especially in the field of cancer rates, the most commonly quoted standard population is the World Standard Population, which is a constructed population, originally due to the late Professor Segi of Nagoya University in Japan: it is designed as an intermediate between the populations of developing countries, which are characterised by a large proportion in the younger age groups, and the European type having a population more evenly divided by age.

The method of standardisation of incidence rates described above is known as the "direct method" (as opposed to the indirect method, which has not been used in this book).

Table 1 illustrates the method of calculation described above. It refers to a population of European type, and shows the reduction in the overall rate because the World Standard Population is of a younger structure.

Table 1.

Age group	Given population (males) Nos. in population	Nos. of cases of cancer	Incidence rate per 100,000	Nos. in World Standard Population	Expected cases in Standard Population
x	P_x	C_x	I_x	W_x	E_x
0-4	14,146	6	42.4	12,000	5.1
5-14	37,096	7	18.9	19,000	3.2
15-24	35,972	11	30.6	17,000	5.2
25-34	33,319	18	54.0	14,000	7.6
35-44	31,848	34	106.6	12,000	12.8
45-54	27,038	102	377.2	11,000	41.5
55-64	25,162	280	1112.8	8,000	89.0
65-74	17,407	345	1982.0	5,000	99.1
75-84	6,545	196	2994.6	1,500	44.9
85+	867	45	5190.3	500	25.9
Total	229,400	1044		100,000	

$I_x = C_x/P_x \times 100,000$

$E_x = I_x \times W_x \div 100,000$

Hence Crude rate = C_x / P_x = 455.1 per 100,000

Standardised rate = E_x / W_x = 334.3 per 100,000

A.2.2 Survival Rates

The simplest form of the survival rate at one year is merely the ratio, expressed in the form of a percentage, of those patients alive a year after their treatment began to all those who were treated (i.e. the survivors and those who died before a year had elapsed). This is known as the "crude survival rate", since no attempt is made to allow for any other factors, such as the age or sex of the patient.

The same procedure is adopted for the second year, whereby the survival rate is calculated as the ratio of those alive two years from the start of their treatment to those alive at the end of one year (and thus eligible to embark on a second year).

The two-year overall survival rate, calculated by what is known as the "actuarial method", is then the product of these two rates. If two years have elapsed for all the patients treated, then this product is the same as the crude two year survival rate calculated as the number alive two years from the start of treatment, divided by the total treated.

In symbolic form, if P_0= No. of patients treated, P_1 = No. of these alive at their first anniversary, and P_2 = No. alive at their second anniversary, then S_1, the one year survival rate, is P_1/P_0, and S_2, the survival rate for the second year, is P_2/P_1. The overall survival rate for two years, $(SR)_2$, is then $S_1 x S_2 = P_1/P_0 \times P_2/P_1 = P_2/P_0$, which is the same as the crude two-year survival rate.

In a corresponding manner, the five-year survival rate, computed actuarially, is obtained by multiplying together five rates, $S_1S_2S_3S_4S_5$, each one probably obtained from successively decreasing totals of patients, but thus utilising the data available to better effect. In this book, a full five-year period of follow up has been available for all patients.

A2.3 Age adjustment of Survival Rates

A group of elderly patients is unlikely to show as high a survival rate as another group, with the same condition and treated in the same way, whose average age is rather younger. Age is in fact one of the most important factors affecting survival rates. It can be allowed for in several ways, the most convenient of which is probably the Life Table Method.

The Life Table (Registrar General, 1979) gives, for each exact age x, and separately by sex, the number of individuals remaining alive (l_x) from a radix (initial number) of 100,000, all considered as having been born at the same time. The "exact" age x is used, rather than the conventional usage (when a stated age refers to any day from the birthday itself to the day before the next birthday

and is thus on average x+1/2), because the Life Table begins at birth which is exact age 0, and proceeds in yearly intervals from then.

Thus l_0 = 100,000, l_{65} = 70,426 and l_{70} = 56,715 (for males, from English Life Table No.13, based on the 1971 Census). This means that out of 70,426 (=l_{65}) men alive at the exact age of 65, 56,715 (=l_{70}) are still alive five years later at the age of 70: for them, therefore, their 5 year survival rate would be l_{70}/l_{65} = 0.8053, or 80.53%.

Since ages are conventionally grouped into five consecutive years, a similar five year Life Table Survival rate for males in the age group 65-69 would be obtained from:-

$$\sum_{x=70}^{74} l_x \Big/ \sum_{x=65}^{69} l_x$$

Which in fact works out to be 251361/326216 = 0.7705, or 77.05%.

The Life Table summarises the effect of all causes of death. For a group of, say, 100 patients in the age group 65-69, we would therefore expect 100x0.7705, which is 77.05 of them, to be alive five years later, if they were to experience the normal pattern of mortality. Taking the actual number who were in this age group at the time treatment began and had survived five years to be say, 30, then the crude five-year survival rate for this group would be 30/100 = 30%, while the age adjusted rate would be 30/77 = 38.94%, because only 77 would be expected to live for five years (from The Life Table).

This adjustment has been made for only a single age group. The same procedure can be extended very easily to cover the entire age range, and is most simply done by computing, from Life Table survival rates calculated as above the separate expectations for each age group, and adding these to give the total number of patients expected to be alive five years later. The actual number of survivors, divided by this total of expected survivors, gives then the age adjusted survival rate. Clearly an exactly analagous procedure can be used for periods different from five years e.g. 10 years, or 1 year, etc.

A more refined method uses the same principle but proceeds one year at a time, and uses the actuarial method for combining successive one-year age adjusted survival rates over long periods. This means that the survival rate for the first year is calculated as the ratio of the number of patients who are alive on their first

anniversary of the start of treatment, to the number of these same patients who would be expected to be alive after the lapse of one year, caculated by the use of the Life Table applied to the composition of the group of patients by age and sex. The number expected to survive for a second year is then calculated from the Life Table applied to the actual survivors, by sex and age (at the end of the first year). This number is then the denominator for obtaining the age adjusted survival rate for the second year, using the number actually surviving to the end of the second year as the numerator. The method is repeated for each successive year, so that the adjustment for age is applied only to the actual survivors, and the five year age adjusted survival rate is the product of the first five such rates. This is the method which has been used in this book.

A2.4 Numerical illustrations.

Suppose that in the original example the number of patients initially treated (P_0) is 500, and that the number (P_1) surviving at their first anniversary is 250, then the one year crude survival rate (S_1) is P_1/P_0 which is 250/500 or 50%. If the number who are alive at their second anniversary is P_2 = 150, then the survival rate (S_2) for the second year is P_2/P_1 = 150/250 which is 60%. Thus the two year survival rate $(SR)_2$ is 150 out of the original 500, which is 30% and is the same as $S_1 x S_2$.

Excerpt from English Life Table No. 13 1970-72

x	l_x	x	l_x
65	70426	70	56715
66	67994	71	53570
67	65400	72	50335
68	62648	73	47038
69	59748	74	43703

For the age group 65-69, the expected (Life Table) one year survival rate is obtained by advancing the age group one year, to 66-70. The sum of the lx figures for 66 to 70 gives the numerator of the fraction, and the sum for 65-69 the denominator. The computation is then the same in principle for each age group. For each successive year of survival, the actual survivors are re-allocated to five year age groups and the same one year Life Table rates used for the calculation of expected numbers of survivors.

If 100 of the 500 patients in the example above were in the age group 65-69, and 55 of them survived to their first anniversary, the adjustment would be made as follows:

$$\sum_{x=66}^{70} l_x \Big/ \sum_{x=65}^{69} l_x = \frac{312\ 505}{326\ 216} = 0.9580$$

0.9580 is the expected one year survival rate for this age group. Thus of 100 patients, 95.8 would be expected to be alive one year later. In fact, there were 55 survivors, for which the adjusted rate would be 55/95.8 = 57.4%, to be compared with 55/100 = 55%.

$$\sum_{x=67}^{71} l_x \Big/ \sum_{x=66}^{70} l_x = \frac{298\ 081}{312\ 505} = 0.9538$$

0.9538 is the expected one year survival rate for the next year, for a group now aged 66-70 to survive to be 67-71. The actual number of survivors was 55, of which 52.46 would be expected to survive (= 55 x 0.9538). If there were 42 survivors to their second anniversary, then their adjusted rate would be 42/52.46 = 80.06% for this second year, compared with 76.36 (42/55) unadjusted.

For the two year period, the number expected to survive out of 100 patients would be 100 x 0.9580 x 0.9538 = 91.37, and 42/91.37 = 45.97, to be compared with an unadjusted rate of 42/100 = 42%.

This example has been confined to a single age group. In practice, the expectations for each age group would be added together to give an overall expected number of survivors to one year, or two years etc., and the actual total of survivors at the same anniversaries would be set against these figures, to provide the appropriate age adjusted survival rate. It is important that the calculation of expected survivors through each year is based on the actual age distribution of the survivors setting out on that year.

Note: In a few tables where the cross tabulations resulted in small numbers in some categories, the effect of age adjustment was to give age adjusted survival rates of over 100% but where this occurred the rates have been "rounded down" to 100.0.

The 1970-72 Life Table has been used rather than the most recent 1980-82 Table because it is nearer to the mid-point of the period (1957-81).

Appendix 3
Census and Inter–censal Populations

Census Populations

Age group	1961		1971		1981	
	Male	Female	Male	Female	Male	Female
0- 4	197,503	186,117	227,630	216,040	161,235	153,258
5- 9	178,969	169,599	227,795	216,275	182,613	171,329
10-14	202,284	192,481	201,965	188,635	222,358	210,100
15-19	184,530	174,739	185,205	172,755	221,139	212,165
20-24	156,434	153,019	196,325	191,220	188,297	182,806
25-29	157,459	148,001	178,735	171,685	172,722	168,484
30-34	168,437	157,978	162,285	151,685	189,871	186,703
35-39	177,925	172,734	153,805	146,300	170,271	165,674
40-44	165,040	163,243	163,330	156,220	153,561	147,602
45-49	170,271	165,531	169,100	166,690	145,155	140,950
50-54	160,698	159,293	153,425	155,030	151,150	147,434
55-59	140,234	144,231	150,505	152,175	150,467	153,718
60-64	105,608	126,437	131,035	142,180	127,040	137,956
65-69	74,420	103,551	101,235	122,225	111,703	129,287
70-74	52,717	80,945	62,540	97,790	82,747	111,231
75-79	33,306	57,846	35,615	68,055	50,660	83,823
80-84	17,795	33,571	18,275	41,375	21,706	50,999
85-89	6,256	13,374	6,930	18,775	7,599	22,987
90-94	1,084	3,045	1,790	5,600	1,972	7,685
95 +	123	518	275	1,060	383	1,769
Total	2,351,093	2,406,253	2,527,800	2,581,770	2,512,649	2,585,960

Inter-censal Populations

Age group	1966		1976	
	Male	Female	Male	Female
0- 4	212,567	201,079	183,400	172,400
5- 9	203,382	192,937	225,200	213,000
10-14	202,124	190,558	228,400	215,600
15-19	184,868	173,747	197,700	189,400
20-24	176,379	172,119	180,100	172,900
25-29	168,097	159,843	197,400	191,200
30-34	165,361	154,832	177,600	169,500
35-39	165,865	159,517	157,000	150,100
40-44	164,185	159,731	152,200	145,600
45-49	169,686	166,111	157,600	152,400
50-54	157,061	157,161	162,100	161,700
55-59	145,370	148,203	146,200	150,700
60-64	118,321	134,309	134,300	144,800
65-69	87,828	112,888	110,600	131,300
70-74	57,628	89,367	76,600	107,800
75-79	34,461	62,951	41,100	76,900
80-84	18,035	37,473	19,400	45,600
85-89	6,593	16,074	7,200	21,500
90-94	1,437	4,323	1,900	7,100
95 +	199	789	400	1,700
Total	2,439,447	2,494,012	2,556,400	2,621,200

Appendix 4

TNM Classification of Malignant Tumours: Larynx (ICD–O 161)

RULES FOR CLASSIFICATION

Classified 1972. Confirmed 1978

The classification applies only to carcinoma.
There should be histological verification of the disease.
Any unconfirmed cases must be reported separately.
The following are the minimum requirements for assessment of the T, N, and M categories.

T categories: Clinical examination, laryngoscopy and radiography.

N categories: Clinical examination.

M categories: Clinical examination and radiography.

ANATOMICAL REGIONS AND SITES

1. Supraglottis (161.1)

   Epilarynx (including marginal zone)

   i) Posterior surface of suprahyoid epiglottis (including the tip).
   ii) Aryepiglottic fold.
   iii) Arytenoid.

   Supraglottis excluding epilarynx

   iv) Infrahyoid epiglottis.
   v) Ventricular bands (false cords).
   vi) Ventricular cavities.

2. Glottis (161.0)

   i) Vocal cords.
   ii) Anterior commissure.
   iii) Posterior commissure.

3. Subglottis (161.2)

REGIONAL LYMPH NODES

The regional lymph nodes are the cervical nodes.

TNM PRE-TREATMENT CLASSIFICATION

T- Primary Tumour

SUPRAGLOTTIS

Tis Pre-invasive carcinoma (carcinoma in situ).

T0 No evidence of primary tumour.

T1 Tumour confined to the region with normal mobility.
T1a Tumour confined to the laryngeal surface of the epiglottis or to an aryepiglottis fold or to a ventricular cavity or to a ventricular band.
T1b Tumour involving the epiglottis and extending to the ventricular cavities or bands.

T2 Tumour confined to the larynx with extension to adjacent site or sites or to the glottis without fixation.

T3 Tumour confined to the larynx with fixation and/or other evidence of deep infiltration.

T4 Tumour with direct extension beyond the larynx.

TX The minimum requirements to assess the primary tumour can not be met.

GLOTTIS

Tis Pre-invasive carcinoma (carcinoma in situ).

T0 No evidence of primary tumour.

T1 Tumour confined to the region with normal mobility.
T1a Tumour confined to one cord.
T1b Tumour involving both cords.

T2 Tumour confined to the larynx with extension to either the supraglottis or the subglottis regions with normal or impaired mobility.

T3 Tumour confined to the larynx with fixation of one or both cords.

T4 Tumour with direct extension beyond the larynx.

TX The minimum requirements to assess the primary tumour can not be met.

SUBGLOTTIS

Tis Pre-invasive carcinoma (carcinoma in situ).

T0 No evidence of primary tumour.

T1 Tumour confined to the region.
T1a Tumour confined to one side of the region.
T1b Tumour with extension to both sides of the region.

T2 Tumour confined to the larynx with extension to one or both cords with normal or impaired mobility.

T3 Tumour confined to the larynx with fixation of one or both cords.

T4 Tumour with destruction of cartilage. and/or with direct extension beyond the larynx.

TX The minimum requirements to assess the primary tumour can not be met.

N - REGIONAL LYMPH NODES

N0 No evidence of regional lymph node involement.

N1 Evidence of involvement of movable homolateral regional lymph nodes.

N2 Evidence of involvement of movable contralateral or bilateral regional lymph nodes.

N3 Evidence of involvement of fixed regional lymph nodes

NX The minimum requirements to assess the regional lymph nodes can not be met.

M - DISTANT METASTASES

M0 No evidence of distant metastases.

M1 Evidence of distant metastases.

MX The minimum requirements to assess the presence of distant metastases can not be met

Note: In this survey, a patient where the extent of the primary, nodes and/or distant metastases were not known (i.e. TX, and/or NX and/or MX), has been classified as "stage not known" (NK), irrespective of which factor could not be assessed.

SUMMARY

GLOTTIS

T1 Limited/mobile.
  a. One cord.
  b. Both cords.

T2 Extension to supra - or sub-glottis/mobile.

T3 Fixation of cord(s).

T4 Extension beyond larynx.

SUPRA - and SUB-GLOTTIS

T1 Limited/mobile.

T2 Extension to glottis/mobile.

T3 Fixation of cord(s).

T4 Extension beyond larynx.

ALL REGIONS

N1 Homolateral movable.

N2 Contra- or bi-lateral movable.

N3 Fixed.

Reference: Union Internationale Contra Le Cancer (UICC). TNM Classification of Maligant Tumours. Third ed 1978. (Reproduced with permission of UICC).

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