British Journal of Cancer (1996) 74, Suppl. XXIX, S54-S60

Cancer clinical outcomes for minority ethnic groups

P Selby

ICRF Cancer Medicine Research Unit, University of Leeds Centre for Cancer Research

Introduction

There has been some work to date, extensively reported in this Symposium, on the epidemiology, service needs and community perspective for minority ethnic groups in the United Kingdom faced with the problem of cancer. A good deal less is known about the clinical outcomes for cancer patients from minority ethnic origins. Until recently Cancer Registries have not recorded ethnic origin in their databases. Hospitals and academic units have also found it difficult to accumulate comprehensive data. However, outcome data is an important element in needs assessment, for service planning and for individual clinicians when faced with patients from minority ethnic groups.

Clinical outcomes are most usually assessed in terms of patients' survival but it is increasingly recognised that an appraisal of outcome must also include consideration of the quality of life during and after cancer treatment. Key clinical questions include the significance of ethnic origin as a factor predicting survival after diagnosis and treatment. This is a multivariate issue and we need to know whether ethnic origin may predict for survival independently or whether it may predict for the stage or distribution of the cancer at diagnosis. This leads on to an analysis of the access of different ethnic groups to medical diagnostic and treatment facilities. Furthermore, if we consider quality of life as a key outcome we need measurement methods suitable for use in all populations. Such instruments need to be evaluated in the relevant populations and, in particular, their validity needs to be assessed across cultures, age groups and ethnic groups.

Work on the significance of ethnic origin in cancer outcomes in the United Kingdom and Europe is not yet extensive. Results, of uncertain generalisable value, from the United States offer the more useful studies available at present.

In this paper the issues of the influence of ethnic origin on survival will be examined mainly drawing on data from the USA. Indications of the problems in the UK and Europe will be given. Methods available for studying quality of life in European patient populations will be briefly reviewed and some indications of future directions of study using these approaches will be given.

The impact of ethnic origin on cancer survival in the United States

In the United States of America differences in survival of cancer patients from different ethnic origin have been demonstrated although the literature tends to focus on the differences between "Black Americans" and "White Americans" often without clarifying the ethnic groups so labelled. White patients have been found to have better survival than black patients during the 1970s and 1980s.[1-10] Most of these early reports showed that white cancer patients had higher survival than black cancer patients even when matched for the stage of the disease found at diagnosis.[1-3,5,7,11-13] The largest differences in survival between white patients and black patients were apparent for cancer of the uterine body, bladder cancer, rectal cancer in men and Hodgkin's disease in women. For all of these sites the difference in relative survival at five years favoured white patients by more than 20% and were still more than 10% after adjustments for age and stage. Smaller but significant differences in the order of 10% were found for colon cancer, breast and rectal cancer among women, prostate, kidney and laryngeal cancer in both sexes and Hodgkin's disease in men.

These observations led the United States National Cancer Institute (NCI) in 1983 to begin a prospective, social and epidemiological study to try to find whether the differences in outcome were biologically or medically determined. The design and data accrual into this important study is described by Howard *et al*[14]. It concentrated on cancers of the uterine body, bladder, breast and colon. Although subsequent data from the Surveillance, Epidemiology and End Results Program[6] suggested some of these differences may be smaller than earlier predicted, the study persevered with these cancer sites. They sought to accrue 1,300 black patients and a similar number of white patients to give the study considerable statistical power. Only Registries capable of collecting data to a very high standard were included in the study.

The investigators sought to confirm the descriptive epidemiology of the ethnic difference and the study became known as the NCI Black/White Cancer Survival Study. They found that blacks tend to have more advanced disease at diagnosis than whites.[2,3,7,8,15-17] Hypotheses to explain the difference in survival and stage at diagnosis included different degrees of investigation of patients to identify their tumour stage, differing tumour grade and biology, differences in factors relating to the host such as nutritional status and immune responses, differences in treatments allocated to the two ethnic groups or differences in compliance with diagnostic tests and treatment. These questions were studied by collection of data from the patients' notes, by interviews and then by prospective follow up. Many of the results of this important study are not yet available but some comments can be made from this and related studies for some cancer sites.

Breast cancer

Ethnic differences in survival from breast cancer were reported for the National Cancer Institute Black/White Cancer Survival Study in the United States by Eley *et al.*[18] They studied 1,130 women (612 black, 518 white) aged 20 to 79 years from Atlanta, New Orleans and San Francisco. Prognostic factors including stage, tumour size, treatment, other medical conditions and social and demographic factors were obtained by a direct personal interview and examination of hospital records. All pathology samples were reviewed. The risk of dying from breast cancer was 2.2 times higher for blacks than for whites which was highly statistically significant. However, the differences in outcome were partly explained by differences in stage at presentation in this study and when corrections for stage were made the excess risk of dying from breast cancer in the black patients was 1.7 times. After adjusting for stage, treatment, other illnesses, pathology, social and demographic features there was still a slightly increased risk of dying among the black patients (1.3 times, 95% confidence limits 1.0-1.8) but this did not achieve statistical significance and treatment did not appear to be an independent contributory factor. It appeared that the most important factor determining survival in the black populations was the more advanced stage at presentation and the authors concluded that this might be amenable to change through improved access to medical care and use of screening facilities.

In subsequent studies, the excess of advanced stage disease in black patients was confirmed and was associated with a history of patient delay, indication of reduced access to health care, lack of

mammograms and, at the margins of statistical significance, income, in explaining the higher stage disease seen in black patients. However, these factors explained only 50% of the variance in stage between the groups.[19] The impact of social ties was considered. In multivariate analysis, absence of close ties and perceived sources of emotional support was associated with an increased death rate from breast cancer in all ethnic groups.[20]

The NCI Study also focused on differences in treatment plans for a sub-group of patients with defined stage of breast cancer, stage II node positive disease.[21] In 305 patients they found similar patient characteristics between the black and white patients although breast conserving surgery was undertaken less frequently among black women (p=0.004). In a multivariate analysis, however, ethnic origin was not a significant factor in determining the selection of primary treatment and this appeared to depend more upon education and metropolitan area of residence. Adjuvant chemotherapy and hormonal therapy was employed in an appropriate degree in all patients studied. Treatment plans do not therefore seem to be determined by ethnic origin but are influenced by education and area of residence.[21]

Length of time from symptom recognition to initial medical consultation was analysed in detail in the NCI Study.[22] This was longer for black women than for white women and this difference approached statistical significance (p = 0.06) but the difference was small at a median of only 16 days. This difference seems unlikely to explain all of the differences in stage at presentation and survival rates in breast cancer.

Colorectal cancer

Black patients with colonic cancer appear to have a poorer survival than white patients in the USA.[23] During 1981-1988, the five year relative survival for white males and females were 59% and 58% respectively whereas for black males and females they were 46% and 49% respectively. This difference is not due to any differences in the site of the cancer within the bowel in black patients.[23] The study identified 1,045 eligible patients and interviewed 71% of these to establish baseline clinical, pathological and demographic/social data as well as diet and occupational data. The results of the survival analysis are recently published with follow up quite mature.[24] Patients were diagnosed in 1985 and 1986 and followed until the end of 1990 (454 black and 521 white). After adjusting for age, sex and geographical area the relative hazard of death was 1.5 in blacks compared to whites with the 95% confidence limits 1.2-1.9. A substantial proportion of the excess risk was due to later stage at presentation among the blacks and, when corrected for this, the hazard ratio was 1.2 (95% limits 1.0-1.5). Further analysis of socioeconomic variables and treatment did not suggest any important influences on outcome, although the data on treatment received lacked detail.

Prostatic cancer

Although not included in the NCI Study, prostatic cancer presents a valuable illustration of studies of the impact of ethnic origin on incidence and outcome. As noted elsewhere in this volume it shows one of the widest ranges of age adjusted incidence of any cancer among different groups and the highest frequency is found in black Americans.[25] The incidence varies from over 90 per 100,000 per year among black Americans in Atlanta, Detroit and Alameda in the United States to less than 10 per 100,000 per year in Singapore, Bombay, Poland, Japan, Hong Kong, Senegal and Shanghai. The rates for white American populations vary between 40 and 60 per 100,000 per year. Age adjusted mortality is much lower than incidence reflecting the large proportion of indolent non-invasive prostatic cancers.[25] The wide variation in prostatic cancer incidence in different populations has not been explained with certainty. High risk populations have been shown to have relatively high serum testosterone levels[26] and case control studies suggest associations of high risk with a number of other factors: high fat intake; a past history of venereal disease; absence of circumcision[27] and family history.[28] The relative risk of prostate cancer among those with a first degree relative with the disease is 3.2 (95% CI 2-5) and the figure is similar in blacks and whites in the USA suggesting that the differences in incidence may be due to environmental factors.

Survival for patients with adenocarcinoma of the prostate in all populations depends heavily upon the stage of the disease and the grade of the tumour. Studies from the United States have indicated important differences in survival between white and black Americans. Austin *et al*[29] and others have demonstrated that black patients have significantly higher tumour grade and stages than white patients. For instance Table I shows the distribution of tumour stage in the different ethnic groups divided according to age, greater or less than 60 years. Table II shows the distribution of tumour grade with the same divisions and here the significant difference is apparent only in the younger patients. These differences were associated with significant differences in survival. Forty eight per cent of the white patients were alive at five years whereas only 35% of the black patients were alive at five years. This difference was particularly apparent in the younger patients.

Table I Age and stage distribution for white and black prostate cancer patients at age greater or less than 60 years

	Clinical Stage			
	B	C	D	
Total				
Black (%)	18	27	55	p < 0.01
White (%)	28	49	23	
Young				
Black (%)	21	21	57	p < 0.05
White (%)	22	67	11	
Old				
Black (%)	17	28	54	p < 0.01
White (%)	31	44	25	

Source: Ref 29.

Table II Age and grade distribution for white and black prostate cancer patients at age greater or less than 60 years

	Gleason grade		
	Low	High	
Total			
Black (%)	47	53	NS
White (%)	63	37	
Young			
Black (%)	36	64	p<0.04
White (%)	89	11	
Old			
Black (%)	58	42	NS
White (%)	50	50	

Source: Ref 29.

There can be many explanations for differences in grade and stage at diagnosis. It may represent an intrinsic difference in the biological aggressiveness of the cancers in the different populations under study. This explanation has been advanced by several authors in reviewing the evidence.[30-32] However, it is possible that attitudes and access to health care can influence the degree of progression apparent at the time of diagnosis of a cancer. In particular, delay in diagnosis may lead to more advanced disease. Austin *et al*[29] have found some evidence of delayed diagnosis with a much higher proportion of white patients seeking medical attention within three months of the onset of symptoms (Table III).

These studies in prostatic cancer are valuable contributions pointing out the need for further work. However, they illustrate the difficulties in investigating the relationship between ethnicity and outcome. First, the definition of "black" is not given in the paper although it is likely that the authors were principally concerned with Americans of African origin. The need for careful definition of the characteristics of the minority ethnic groups under study has been emphasised elsewhere in this volume. Second, the numbers studied are small with only 117 patients in the key study of Austin *et al*.[29] This is inadequate to allow any precision in the statistical estimates and most importantly does not allow multivariate analysis to be carried out with confidence.

Table III Age and delay distribution for white and black prostate cancer patients at age greater or less than 60 years

	Patient delay in seeking medical attention		
	≤ 3 months	> 3 months	
Total			
Black (%)	58	42	p<0.007
White (%)	87	13	
Young (%)	69	31	NS
Old (%)	72	28	
Young			
Black (%)	28	72	p<0.005
White (%)	100	0	
Old			
Black (%)	64	36	NS
White (%)	82	18	

Source: Ref 29.

Third, outcome is only considered in terms of survival without consideration of quality of life. Even for this common and increasing cancer where social, cultural, environmental and ethnic factors have had a high profile because of the wide range of incidence, we still cannot define the significance of each of these different elements in determining outcome in an advanced Western society. Further studies to characterise the relationship between outcome and the primary characteristics of the patient, the presenting characteristics of the tumour and those factors which influence the timing and quality of health care are essential.

Choice of treatment for prostate cancer may be influenced by ethnic origin. In a study of the treatment of prostatic cancer in black and white Americans in Connecticut, Polednak and Flannery[33] studied the population based cancer registry and identified the first course of treatment used for each stage of prostatic cancer for blacks and whites. A higher proportion of black patients were diagnosed with metastatic disease (35.4% versus 22.1 %) with a higher age specific incidence rate for metastatic cancer among the black patients. There was no identified difference in histological grade. There was a significantly lower use of prostatectomy in black patients than in white patients younger than 70 years of age. There was no difference in the use of hormonal therapy or endocrine surgery. The significance of the difference in prostatectomy rate in determining survival was not clear in this study.

The European perspective - variations in outcome between countries

In Figures 1 and 2 the incidence and mortality for cancer excluding epithelial skin cancers, in men and women in the European Community are given.[34,35] Between nations the risk of dying from cancer in the European Community is highest in Luxembourg, Belgium, France and the Netherlands and lowest in Portugal, Greece, Spain and Ireland. The difference is quite large and the incidence of cancer overall is 55% higher among the French than among the Portuguese, for instance. Men are more likely to die of cancer than women. The patterns of cancer also vary between countries.

There is no precision to the patterns between countries but in general lung cancer is especially common in the northern part of Europe together with rectal cancer whereas in the southern part of Europe cancers of the upper part of the intestines, the throat and the liver are more frequent. Some of these differences are well understood and reflect known causative factors such as tobacco and alcohol. Skin type reflecting ethnic origins is an important factor in determining the risk of malignant melanoma. Although exposure to sun and therefore potential for sunburn is much greater in the southern part of Europe, malignant melanoma there is less common. The people who appear to suffer from malignant melanoma are those of light complexion of northern Europe with a history of sunburn or chronic sun exposure.

Figures 1 and 2 give crude indications of variation in outcome for cancer patients across Europe by comparing incidence with mortality. However, more detailed studies are necessary to characterise this more fully and allow any assessment of the impact of the varying ethnic make-up of different European countries. In the recent Eurocare study[36] data were taken from 30 population based cancer registries across Europe describing outcomes for 800,000 cancer patients diagnosed between 1978 and 1985. Relative survival corrected for age was reported for 25 cancer sites. There was considerable variation between countries and it was notable that the UK had lower survival than most other European countries for 18 of the 25 sites analysed. Scotland fared rather worse than England. Better than average results were apparent in the Swiss, Finnish and Danish registry outcomes for survival. The explanations for the variations remain uncertain. Detailed information about the mix of cases in the different registries is yet to be established and many factors influence outcomes. European countries have very varying policies for screening for cancer, in diagnostic services, and in the ascertainment of death in their registries. In the context of our current discussion, there are different ethnic mixes between different European countries. Ongoing studies will clarify the importance of these different factors.

The European data therefore point to considerable variation in incidence, mortality and survival between different European countries. They present many questions about the significance of differences in ethnic mix in determining outcome but they do not yet answer the questions posed.

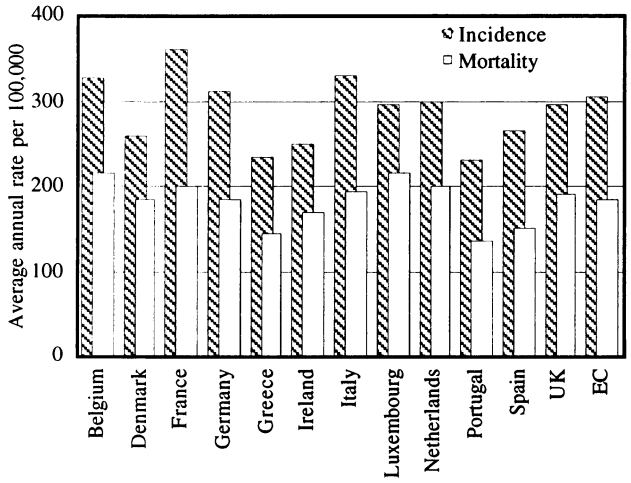

Figure 1 Estimated incidence and mortality for all cancer in men except skin cancers

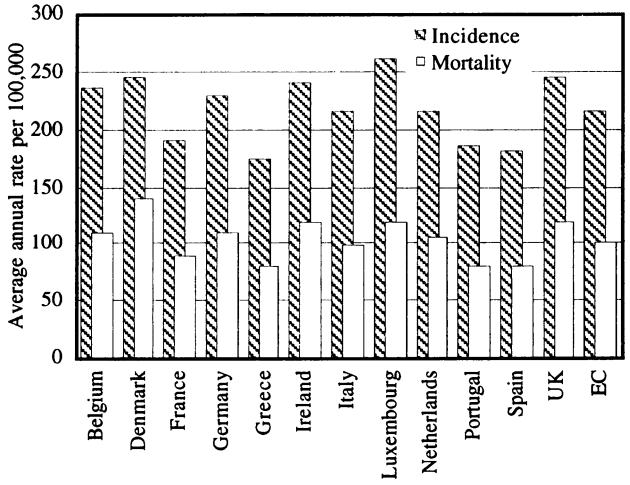

Figure 2 Estimated incidence and mortality for all cancer in women except skin cancers

Quality of Life

If we are to adequately assess outcomes for minority ethnic groups treated for cancer in the UK, careful consideration will have to be given to methods of measuring quality of life. There has been significant general advance in this area.

In 1975 the evaluation of quality of life (QL) in cancer medicine was a rarity. Since that time several groups have worked to develop appropriate measurement methods for this important outcome variable. Different groups have defined the concept in different ways but the essential themes of health related quality of life have always included a psychological dimension, a physical and functional dimension and often additional dimensions including a wide range of specific items relating to the disease in question, particularly symptoms and broader items addressing social and spiritual issues. There are a wide range of prominent clinical trials groups in North America[37-40] and in Europe[41-44] national and international cancer institutes and societies,[45-47] regulatory agencies[48] and the pharmaceutical industry[49] involved in this work. In randomised trials, quality of life has now been evaluated in many cancers including breast cancer,[50-54] lung cancer[55,56] and soft tissue sarcoma.[57] Every clinical trial organisation now recognises the importance of the evaluation of quality of life but it is still not routinely available in every trial.[58,59] The difficulties of evaluating quality of life have in the past been very substantial.[60,61] There has been a reluctance to accept this aspect of outcome evaluation in many clinical communities. The absence of satisfactory measurement methods was a barrier for many years.

The need for instruments to measure quality of life in cancer patients that were psychometrically robust (reliable and valid), concise and widely accepted led to research on their development by a number of groups. In Canada, Schipper and colleagues[62] and Selby and colleagues[63] developed cancer specific questionnaires

Figure 3 HAD Scale

Initials:___ Patient No:_____ Date:____Visit No:_____

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he will be able to help you more.

This questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling in the past week

Don t take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought-out response.

Tick only one box in each section

I feel tense or 'wound up':	**I feel as if I am slowed down:**
Most of the time ☐	Nearly all the time ☐
A lot of the time ☐	Very often ☐
Time to time, Occasionally. ☐	Sometimes ☐
Not at all ☐	Not at all ☐
I still enjoy the things I used to enjoy:	**I get a sort of frightened feeling like'butterflies' in the stomach:**
Definitely as much ☐	Not at all ☐
Not quite so much ☐	Occasionally ☐
Only a little ☐	Quite often ☐
Hardly at all ☐	Very often ☐
I get a sort of frightened feeling as if something awful is about to happen:	**I have lost interest in my appearance:**
Very definitely and quite badly ☐	Definitely ☐
Yes, but not too badly ☐	I don't take so much care as I should ☐
A little, but it doesn't worry me ☐	I may not take quite as much care ☐
Not at all ☐	I take just as much care as ever ☐
I can laugh and see the funny side of things:	**I feel restless as if I have to be on the move:**
As much as I always could ☐	Very much indeed ☐
Not quite so much now ☐	Quite a lot ☐
Definitely not so much now ☐	Not very much ☐
Not at all ☐	Not at all ☐
Worrying thoughts go through my mind:	**I look forward with enjoyment to things:**
A great deal of the time ☐	As much as ever I did ☐
A lot of the time ☐	Rather less than I used to ☐
From time to time but not too often ☐	Definitely less than I used to ☐
Only occasionally ☐	Hardly at all ☐
I feel cheerful:	**I get sudden feelings of panic:**
Not at all ☐	Very often indeed ☐
Not often ☐	Quite often ☐
Somet imes ☐	Not very often ☐
Most of the time ☐	Not at all ☐
I can sit at ease and feel relaxed:	**I can enjoy a good book or radio o TV programme:**
Definitely ☐	Often ☐
Usually ☐	Sometimes ☐
Not often ☐	Not often ☐
Not at all ☐	Very seldom ☐

Figure 4 EORTC QLQ-C30

We are interested in some things about you and your health. Please answer all of the questions yourself circling the number that best applies to you. There are no "right" or 'wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:_____
Your birthdate (Day, Month, Year):_____
Today's date (Day, Month, Year):_____

	No	Yes
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2
2. Do you have any trouble taking a long walk?	1	2
3. Do you have any trouble taking a short walk outside of the house?	1	2
4. Do you have to stay in a bed or a chair for most of the day?	1	2
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2
6. Are you limited in any way in doing either your work or doing household jobs?	1	2
7. Are you completely unable to work at a job or to do household jobs?	1	2

During the past week:	**Not at all**	**A little**	**Quite a bit**	**Very much**
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. H ave you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you:

29. How would you rate your overall physical condition during the past week?

1 2 3 4 5 6 7
Very poor Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7
Very poor Excellent

with many of the features necessary for measuring quality of life in cancer patients. In the United Kingdom, Priestman and Baum[64] introduced the use of linear analogue scales for this purpose. The European Organisation for Research and Treatment of Cancer Study Group on Quality of Life initiated a research programme in 1986 to develop an integrated measurement system for evaluating the quality of life of patients participating in international clinical trials. Drawing on a wide experience within the group and on the previous attempts they developed a modular approach to quality of life assessment.[65] Their core questionnaire, now known as the QLQ-C30, incorporates a range of physical, emotional and social health issues relevant to the broad range of cancer patients irrespective of specific diagnosis and this is supplemented by disease specific and/or treatment specific questionnaire modules.[66] This latter approach by the EORTC Study Group has been evaluated especially widely and thoroughly[67] and in several languages.

In 1989, a Working Party of the Medical Research Council (UK) evaluated all of the questionnaires for measuring quality of life developed during the 1970s and 1980s. Maguire and Selby[68] in reporting this evaluation recommended that at that time two questionnaires probably represented the "best buy". These were the Rotterdam Symptom Checklist developed by de Haes *et al*[69] in Holland and the Hospital Anxiety and Depression Scale developed by Snaith in Leeds.[70] These questionnaires had suitable psychometric properties for assessing a broad range of items relevant to quality of life (the Rotterdam Symptom Checklist) or specifically for quantifying anxiety and depression (the Hospital Anxiety and Depression Scale). Since the evaluation of Maguire and Selby,[68] the EORTC QLQ-C30 has been introduced, extensively evaluated and achieved wide acceptance. Figures 3 and 4 show the Hospital Anxiety and Depression Scale and the EORTC QLQ-C30 core questionnaire.

These methods need to be rigorously evaluated and used in studies of differing outcomes for cancer patients in the United Kingdom. They represent special challenges within minority ethnic groups where language may be a barrier for some and where cultural, social and educational differences may need to be very carefully considered to allow useful information to be gained in order to improve services without burdening patients.

Conclusion

In this paper I have sought to indicate the importance of the evaluation of clinical outcomes in minority ethnic groups and to give examples of studies from the United States, perhaps drawing attention to the lack of studies in the UK. We can conclude that minority ethnic groups have significantly poorer cure rates for some cancers and that diagnosis at a more advanced stage is one factor causing this in some cancers. Differing responses to, and access to, health care systems may be factors in reducing the chance of cure in some circumstances. Illustration is given of methods that can be used, after further evaluation, to study quality of life as an appropriate outcome. This paper does little more than indicate the need for further study but the methods to be employed for analysis of prognostic factors and quality of life are now well established and familiar in clinical cancer research. Benefits to patients from minority ethnic groups in terms of survival and quality of life may be anticipated from more precise evaluation of outcomes in these groups and the factors which influence these outcomes. It is timely to study this aspect of cancer care in the UK.

References

1. YOUNG JL, RIES LG, POLLACK ES. (1984) Cancer patients survival among ethnic groups in the United States. *J of the National Cancer Institute* **73**; 341-352.
2. MYERS MH & HANKEY BF. (1980) Patient Survival Experience. *NIH Publication* **80**; 2148.
3. AXTELL LM, MYERS MH, SHAMBAUGH EM. (1975) *Treatment and survival patterns for black and white cancer patients diagnosed 1955-1964.* Department of Health, Education and Welfare (DHEW) Publication No (NIH) **75**; 712.
4. AXTELL LM & MYERS MH.(1978) Contrasts in survival of black and white cancer patients 1960-1973. *J Natl Cancer Inst.* **60**; 1209-1215 .
5. AXTELL LM, ASIRE AJ, MYERS MH (eds) (1981) *Cancer patient survival: Report No 5.* NIH Publication No **81**; 992.
6. RIES LG, POLLACK ES, YOUNG JL Jr. (1983) Cancer patient survival: Surveillance, Epidemiology and End Results Program 1973 -1979. *J Natl Cancer Inst.* **70**; 693-707.

7a. METTLIN C, NATARAJAN N, MURPHY GP. (1982) Recent patterns of care of prostate cancer patients in the United States: Results from the surveys of the American College of Surgeons Commission on Cancer. *International Advances in Surgical Oncology* **5**; 277-321.

7b. METTLIN C, NATARAJAN N, MITTELMAN A *et al.* (1982) Management and survival of adenocarcinoma of the rectum in the United States: Results of a national survey by the American College of Surgeons. *Oncology* **39**; 265-273.

8. MURPHY GP, NATARAJAN N, PONTES JE *et al.* (1982) The national survey of prostate cancer in the United States by the American College Surgeons. *J of Urology* **127**; 928-934.
9. CHRISTOPHERSEN WM AND NEALON NA. (1981) Uterine cancer: A comparative study of black and white women. In Mettlin C, Murphy GP eds. *Cancer Among Black Populations: Progress in Clinical and Biological Research Vol 53*, New York: Alan R Liss; 185-195.
10. SHAPIRO S, VENET W, STRAX P *et al.* (1982) Prospects for eliminating racial differences in breast cancer survival rates. *Am J of Public Health* **72**; 1142-1145.
11. KOVI J, VIOLA MV, CONNOLLY CA *et al.* (1974) Gastric cancer in American negroes. *Cancer* **34**; 765-770.
12. STEINHORN SC, MYERS MH, HANKEY BF *et al.* (1986) Factors associated with survival differences between black women and white women with cancer of the uterine corpus. *Am J of Epidemiology* **124**; 85-93.
13. WHITE JE, ENTERLINE JP, ALAM Z *et al.* (1981) Cancer among blacks in the United States: Recognising the problem. In Mettlin C, Murphy GP eds. *Cancer Among Black Populations: Progress in Clinical and Biological Research Vol* **53,** 35-53. Alan R Liss: New York.
14. HOWARD J, HANKEY BF, GREENBERG RS *et al* (1992) A collaborative study of differences in the survival rates of black patients and white patients with cancer. *Cancer* **69**: 2349-2360.
15. NEMOTO T, VANA J, NATARAJAN N *et al.* (1981)Observations on short term and long term surveys of breast cancer by the American College of Surgeons: I Significance of the number of axillary nodes and II Estrogen receptor assay in the US in 1977. *International Advances in Surgical Oncology* **4**; 209-239.
16. FOWLER WC JR, FREEMAN AC, HULKA BS *et al.* (1984) Delays in cervical cancer treatment: An assessment of patient and provider characteristics. eds Engstrom PF, Anderson PN, Mortenson LE. In *Advances in Cancer Control: Epidemiology and Research. Progress in Clinical and Biological Research Vol 156*, 265-274. Alan R Liss: New York.
17. POLEDNAK AP. (1986) Breast cancer in black and white women in New York state: Distribution and incidence rates by clinical stage at diagnosis. *Cancer* **58**; 807-815.
18. ELEY JW, HILL HA, CHEN VW, AUSTIN DF, WESLEY MN, MUSS HB, GREENBERG RS, COATES RJ, CORREA P, REDMOND CK *et al.* (1994) Racial differences in survival from breast cancer: Results of the

National Cancer Institute Black/White Cancer Survival Study. *J of the Am Medical Association* **272;** 947-954.
19. HUNTER CP, REDMOND CK, CHEN VW, AUSTIN DF, GREENBERG RS, CORREA P *et al.* (1993) Breast cancer factors associated with stage at diagnosis in black and white women. Black/White Cancer Survival Study Group. *J Natl Cancer Inst.* **85**; 1129-1137.
20. REYNOLDS P, BOYD PT, BLACKLOW RS, JACKSON JS, GREENBERG RS, AUSTIN DF *et al.* (1994) Relationship between social ties and survival among black and white breast cancer patients. National Cancer Institute Black/White Cancer Survival Study Group. *Cancer Epidemiology, Biomarkers & Prevention* **3**; 253-259.
21. MUSS HB, HUNTER CP, WESLEY M, CORREA P, CHEN VW, GREENBERG RS *et al* (1992) Treatment plans for black and white women with stage II node positive breast cancer. National Cancer Institute Black/White Cancer Survival Study Experience. *Cancer* **70**; 2460-2467.
22. COATES RJ, BRANSFIELD DD, WESLEY M, HANKEY B, ELEY JW, GREENBERG RS *et al.* (1992) Differences between black and white women with breast cancer in time from symptom recognition to medical consultation. Black/White Cancer Survival Study Group. *J Natl Cancer Inst.* **84**; 938-950.
23. COATES RJ, GREENBERG RS, LIU MT, CORREA P, HARLAN LC, REYNOLDS P, FENOGLIO-PREISER CM *et al.* (1995) Anatomic site distribution of colon cancer by race and other colon cancer risk factors. *Diseases of the Colon & Rectum* **38**; 42-50.
24. MAYBERRY RM, COATES RJ, HILL HA, CLICK LA, CHEN VW, AUSTIN DF *et al.* (1995) Determinants ofblack/white differences in colon cancer survival. *J Natl Cancer Inst.* **87**;1686-1693.
25. MUIR CS, NECTOUX J A& STASZEWSKI J. (1991) The epidemiology of prostatic cancer: Geographical distribution and time trends. *Acta Oncologica* **30**; 2: 133-144.
26. ROSS R, BERNSTEIN L, JUDD H *et al.* (1986) Serum testosterone levels in healthy young black and white men. *J Natl Cancer Inst.* **76**; 1: 45-48.
27. ROSS R, SHIMIZU H, PAGANINI-HILL A *et al.* (1987) Case control studies of prostate cancer in blacks and whites in Southern California. *J Natl Cancer Inst.* **78**; 5: 869-873 .
28. HAYES RB, LIFF JM, POTTERN LM, GREENBERG RS, SCHOENBERG JB, SCHWARTZ AG, SWANSON GM, SILVERMAN DT, BROWN LM, HOOVER RN *et al.* (1995) Prostate cancer risk in US blacks and whites with a family history of cancer. *International J of Cancer* **60**; 3: 361-4.
29. AUSTIN J-P, AZIZ H, POTTERS L, THELMO W, CHEN P, CHOI K *et al.* (1990) Diminished survival of young blacks with adenocarcinoma of the prostate. *Am J of Clinical Oncology* **13**; 6: 465-469.
30. OWEN WL. (1976) Cancer of the prostate: A literature review. *Journal of Chronic Diseases* **29**;89.
31. BURBANK F AND FRAUMENI JF Jr. (1972) US cancer mortality: Non-white predominance. *J Natl Cancer Inst.* **49**; 649-53.
32. LEVINE RL AND WILCHINSKY M. (1979) Adenocarcinoma of the prostate: A comparison of the disease in blacks versus whites. *J of Urology* **121**; 761-2.
33. POLEDNAK AP & FLANNERY JT. (1992) Black vs white racial differences in clinical stage at diagnosis and treatment of prostatic cancer in Connecticut. *Cancer* **70**; 2152-2158.
34. JENSEN OM, ESTEVE J, MOLLER H *et al.* (1990) Cancer in the European Community and its member states. *EJC* **26**; 1167-256.
35. WHEELER S AND SELBY P. (1993) *Confronting Cancer-cause and prevention.* Penguin Books, London.
36. BERRINO F, SANT M, VERDECCHIA A, CAPOCACCIA R, HAKULINEN T, ESTEVE J (1995). *Survival of Cancer Patients in Europe. The EUROCARE Study.* IARC Scientific Publication No 132, Lyon.
37. MOINPOUR CM, FEIGL P, METCH B *et al.* (1989) Quality of life end points in cancer clinical trials: review and recommendations. *J Natl Cancer Inst.* **81**; 485-495.
38. KORNBLITH AB, ANDERSON J, CELLA DF *et al.* (1990) Quality of life assessment of Hodgkin's disease survivors: a model for cooperative clinical trials. *Oncology* **4**; 93-101.
39. FINKELSTEIN DM, CASSILETH BR, BONOMI PD *et al.* (1988) A pilot study of the Functional Living Index - Cancer (FLIC) scale for the assessment of quality of life for metastatic lung cancer patients. An Eastern Cooperative Oncology Group Study. *Am J of Clinical Oncology* **11**; 630-633.
40. OSOBA D. (1992) The Quality of Life Committee of the Clinical Trials Group of the National Cancer Institute of Canada: organisation and functions. *Quality of Life Research* **1**; 203-211.
41. AARONSON NK AND BECKMANN J. (1987) *The Quality of Life of Cancer Patients.* EORTC Monograph Series 17; Raven Press: New York.
42. AARONSON NK, VAN DAM FSAM, POLAK CE *et al.* (1986) Prospects and problems in European psychosocial oncology: a survey of the EORTC Study Group on Quality of Life. *J of Psychosocial Oncology* **4**; 43-53.
43. GANZ PA, BERNHARD J, HURNY C. (1991) Quality of life and psychosocial oncology research in Europe: state of the art. *J of Psychosocial Oncology* **9**; 1-22.
44. GELBER RD AND GOLDHIRSCH A. (1986) A new endpoint for the assessment of adjuvant therapy in postmenopausal women with operable breast cancer. *J of Clinical Oncology* **4**; 1772-1779.
45. NAYFIELD SG AND HAILEY BJ. (1991) *Quality of Life Assessment in Cancer Clinical Trials.* Division of Cancer Prevention and Control. National Cancer Institute: Bethesda MD.
46. AMERICAN CANCER SOCIETY. (1991) American Cancer Society's Second Workshop on methodology in behavioural and psychosocial cancer research. *Cancer* **67**.
47. STJERNSWARD J AND TEOH N. (1991) Perspectives on quality of life and the global cancer problem. In *Effect of Cancer on Quality of Life.* Osoba D (ed). 1-5. CRC Press: Boston.
48. JOHNSON JR AND TEMPLE R. (1985) Food and Drug Administration requirements for approval of new anticancer drug. *Cancer Treatment Reports* **69**; 1155-1159.
49. HENDERSON-JAMES D AND SPILKER B. (1990) An industry perspective. In *Quality of Life Assessment in Clinical Trials.* Spilker B (ed). 183-192. Raven Press: New York.
50. KIEBERT GM, DE HAES JC, VAN DE VELDE CJ. (1991) The impact of breast conserving treatment and mastectomy on the quality of life of early stage breast cancer patients: a review. *J of Clinical Oncology* **9**; 1059-1070.
51. IRVINE D, BROWN B, CROOKS D *et al.* (1991) Psychosocial adjustment in women with breast cancer. *Cancer* **67**; 1097-1117.
52. GOLDHIRSCH A, GELBER RD, SIMES RJ *et al.* (1989) Costs and benefits of adjuvant therapy in breast cancer: a quality adjusted survival analysis. *J of Clinical Oncology* **7**; 36-44.
53. COATES A, GEBSKI V, BISHOP JF *et al.* (1987) Improving the quality of life during chemotherapy for advanced breast cancer: a comparison of intermittent and continuous treatment strategies. *New England J of Medicine* **317**; 1490-1495.
54. VAN HOLTEN-VERZANTVOORT AT, ZWINDERMAN AH, AARONSON NK *et al.* (1991) The effect of supportive pamidronate treatment on aspects of quality of life of patients with advanced breast disease. *EJC* **27**; 544-549.
55. GEDDES DM, DONES L, HILL E *et al.* (1990) Quality of life during chemotherapy for small cell lung cancer: assessment and use of a daily diary card in a randomised trial. *EJC* **26**; 484-492.

56. GANZ PA, LEE JJ, SIAU J. (1991) Quality of life assessment: an independent prognostic variable for survival in lung cancer. *Cancer* **67**; 3131-3135.
57. SUGARBAKER PH, BAROFSKY 1, ROSENBERG SA *et al.* (1982) Quality of life assessment of patients in extremity sarcoma clinical trials. *Surgery* 91; 17-23.
58. VELDHUYZEN VAN ZANTEN SJ. (1991) Quality of life as outcome measures in randomised clinical trials: an overview of three general medical journals. *Controlled Clinical Trials* **12**; 234S-242S.
59. O'YOUNG J AND MCPEEK B. Quality of life variables in surgical trials. *J of Chronic Diseases* **40**; 513-522
60. DEYO RA AND PATRICK DL. (1989) Barriers to the use of health status measures in clinical investigation, patient care and policy research. *Medical Care* **27**; S254-268.
61. YANCIK R, EDWARDS BK, YATES JW. (1989) Assessing the quality of life of cancer patients: practical issues in study implementation. *J of Psychosocial Oncology* **7**; 598-74.
62. SCHIPPER H, CLINCH J, MCMURRAY A *et al.* (1984) Measuring the quality of life of cancer patients. The Functional Living Index - Cancer: development and validation. *J of Clinical Oncology* **2**; 472-483.
63. SELBY P, CHAPMAN J W, BOYD N F. (1984) Methods of evaluating quality of life in cancer patients. *BJC* **49**; 386-387.
64. PRIESTMAN T AND BAUM M. (1976) Evaluation of quality of life in patients receiving treatment for advanced breast cancer. *Lancet* **1**; 899-900.
65. AARONSON NK, AHMEDZAI S, BERGMAN B *et al.* (1993) The European Organisation for Research and Treatment of Cancer QLQ-C30; a quality of life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst.* **85**; 5: 365-375.
66. SPRANGERS MAG, CULL A, BJORDAL K. (1993) The European Organisation for Research and Treatment of Cancer approach to quality of life assessment: guidelines for developing questionnaire modules. *Quality of Life Research* **2**; 287-295.
67. AARONSON NK, CULL A, KAASA S *et al* (1995) The European Organisation for Research and Treatment of Cancer modular approach to quality of life assessment in oncology: an update. In *Quality of Life and Pharmacoeconomics in Clinical Trials, 2nd edition.* Ed Spilker B. Raven Press:New York. In press.
68. MAGUIRE P AND SELBY P. (1989) Assessing the quality of life in cancer patients. *BJC* **60**; 437-440.
69. DE HAES JCJM, VAN KNIPPENBERG FCE, NEIJT JP. (1990) Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *BJC* **62**; 1034-1038.
70. ZIGMOND A AND SNAITH P. (1983) The Hospital Anxiety and Depression Questionnaire. *Acta Scand Psychiat* **67**; 361-368.