Possible explanations for social class differences in cancer patient survival

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Social class differences in cancer patient survival have been reported for most cancer types and for a number of countries. The etiology of these differences has been studied less thoroughly and less systematically than social class differences in cancer occurrence. Stage of disease at diagnosis appears to be the most important factor contributing to the social class differences in cancer patient survival. This has been observed most clearly for gastrointestinal and gynaecological cancers. Social class differences in survival are generally wider for patients diagnosed with cancer at local stages than for those diagnosed with cancer at advanced stages. The reasons why cancers are more frequently diagnosed at a local stage in high than in low social classes is not properly understood at the moment. Of other potential contributing factors, the role of treatment and psychosocial factors has scarcely been studied. Biological indicators of tumour aggressiveness have failed to explain the social class differences.

There is a great deal of evidence that cancer patients from lower social classes* do worse than those who are more privileged (see the chapter by Faggiano et al. in this book). These differences seem to exist in all societies where comparisons of survival rates by social class have been made. Differences in cancer patient survival are not due to the direct effect of social class, but rather to intervening factors, i.e. intermediate causal steps. Most studies have failed to reveal the reasons for the differences in survival. There are two main explanations for this. First, the concept of social class is complex. It cannot be observed or measured directly but only by using surrogate measures. The different operational definitions used succeed, at best, in covering only a few aspects of the concept of social class. Further discussion on this topic can be found in chapters elsewhere in this book. Second, many studies have been limited to describing the existence of survival differences, and have not examined their causes.

Stage at diagnosis is the most important factor contributing to social class differences in cancer patient survival. Nevertheless, its role seems to vary

*In our article, the term social class is used to cover several aspects, including occupation, income and education, which are also sometimes referred to as socioeconomic status or sociodemographic status.

widely by type of tumour and possibly also by country. Stage at diagnosis has a clear influence on social class differences in survival from stomach and colon cancer, whereas its role is more modest in rectum, breast, cervix and bladder cancer. Social class differences in survival appear to be more prominent among patients diagnosed with cancer at a local stage than among those diagnosed at more advanced stages. The factors explaining differences in stage distribution by social class are not well known. Delay of diagnosis does not appear to contribute substantially to social class differences in cancer survival. Nor do tumour characteristics explain survival differences by social class.

Social class differences in cancer treatment have also been reported and, in some instances, they have contributed to survival differences. However, a prerequisite for studying the effect of treatment has been that there are residual differences after adjustment for stage. Thus, the handful of studies published on the role of treatment should be interpreted in a wider context.

Empirical identification of the factors contributing to social class differences in survival should be a research priority, as it is prerequisite to developing interventions that diminish such inequalities.

Comprehensive explanations

Berg *et al.* (1977), Vågerö and Persson (1987), and Leon and Wilkinson (1989) have provided lists of possible explanations for the etiology of social class differences in cancer survival. Berg *et al.* (1977), the first to offer such a systematic account, suggested that when there are no differences in treatment, social class differences in survival might be due to differences in when medical help is sought, in the general health and life expectancy of the patients, or in the cancer–host interaction and behaviour of the cancer.

Vågerö and Persson (1987) have provided the most complete list of explanations for survival differences. Their list – cited here – covers both causal and non-causal explanations:

(1) Early detection of cancer (without real improvement of prognosis) is more common in white collar workers.

(2) Early detection of cancer (with some real improvement of prognosis) is more common in white collar workers.

(3) Differential treatment resulting in differential prognosis favours white collar workers.

(4) Differences attributable to host factors influence body susceptibility or body response to cancer.

(5) There are differences attributable to the biological properties of the tumours compared, for instance, with the distribution of histologic types for a particular cancer localization.

Subsequent lists of possible explanations, presented by a number of authors, have been more or less modifications of the account by Vägerö and Persson (1987). To summarize, these theories suggest that the differences, if they are not artifactual, are related to the tumour, patient and/or health care.

Artifactual explanations

Lead-time bias The claim that social class differences in cancer patient survival are artifactual implies that patients having a higher social status have not really gained a true survival advantage. As Vågerö and Persson (1987) indicated, at least part of the survival advantage of earlier diagnosis is artificial: the time of diagnosis is advanced but the death is not delayed – that is, treatment does not alter the natural history of the disease. In its general form, the problem of lead-time bias was pointed out for the first time more than 30 years ago (Saxén & Hakama 1964; Hutchinson & Shapiro, 1968) and was already discussed at length (Enstrom & Austin, 1977) in the 1970s. Efforts to overcome the effects of the problem have been made (Jacques *et al.*, 1981), but the problem has been comprehensively addressed mainly in the field of screening (Miller, 1985). Obviously, earlier diagnosis can give a real survival advantage by changing the natural history of the disease and, thus, postponing death.

The problem of lead-time bias could be tackled by calculating survival time from the first symptom instead of the verification of diagnosis. This approach cannot, however, be applied when dealing with cancers detected at a symptomless stage (for example, cancers detected through organized screening programmes, in medical check-ups or as a chance finding resulting from investigation due to an unrelated disease). Furthermore, it is possible that perception, recall and reporting of symptoms may vary by social class (Mechanic, 1972; Funch, 1988). Another approach is to use stage of disease at diagnosis as a proxy for lead-time and stratify by stage.

The role of lead-time – that is, delay in diagnosis - in the occurrence of social class differences in cancer survival has been assessed by Savage et al. (1984) in myeloma and by Auvinen (1992). Time from first symptom was longer among lower social classes in both studies, but the differences were not statistically significant and delay did not contribute materially to social class differences in survival. In a study in Italy among colon cancer patients, delay in diagnosis did not seem to account for the differences in distribution of stage at diagnosis with social class (Vineis et al., 1993). Furthermore, no prognostic impact of delay has been observed in some studies on breast cancer (Neave et al., 1990; Porta et al., 1991) and colorectal cancer (Barillari et al., 1989; Porta et al., 1991), although in breast cancer contrasting results have also been reported (Wilkinson et al., 1979; Machiavelli et al., 1989).

Diagnostic practices may affect the survival differences between social classes in another way. People from higher social classes tend to use health care services more regularly. It is possible that frequent and extensive check-ups result in rather benign tumours being diagnosed more often in higher than lower social classes. Since these tumours do not cause deaths, they contribute to high survival rates in higher social classes.

Confounding Careful consideration is needed to determine whether a prognostic factor should be considered a confounder, an effect modifier or an explanatory variable in analyses. In the early literature, even stage of disease has been taken as a confounder instead of an explanatory variable (for example: Linden, 1969; Lipworth *et al.*, 1972; Keirn & Metter, 1985).

Clearly, factors such as age and calendar date of diagnosis should be treated as confounders. However, studying their possible effect modification might be of interest. For example, Karjalainen and Pukkala (1990) reported more marked social class differences in cancer survival among patients at older ages. The social class differences could also change over time: either by calendar period of diagnosis or with period of follow-up after diagnosis. There is some evidence that as the excess risk of death due to cancer decreases in longer follow-up, the social class differences also diminish or disappear (Karjalainen & Pukkala, 1990).

The roles of other demographic factors in addition to age – for example, marital status, race, urbanity, and place of residence - require further consideration. They are often correlated to both social class and survival, and thus easily regarded as confounders at first glance. The relationship of race and social class provides an example of this dilemma. African/American ethnic origin is correlated with low social class in the United States of America. It is difficult to establish which factor is of primary importance in analysis of cancer patient survival. Empirical results have been contradictory. In some studies, racial differences have disappeared after controlling for social class; this has been observed in breast cancer (Dayal et al., 1982; Bassett & Krieger, 1986; Stavraky et al., 1987; Gordon et al., 1992) and in prostate cancer (Dayal & Chiu, 1982; Dayal et al., 1985). The reverse pattern has been reported in colorectal cancer: controlling for race abolished social class differences (Daval et al., 1987). In yet another study, social class explained some of the racial differences, but not all of them (Wegner et al., 1982). The confusion is not made any clearer by the fact that in some studies race has even been used as a surrogate for social class (Page & Kuntz, 1980).

However, the role of the demographic factors in

relation to social class cannot be assessed solely on the basis of correlation between the variables. Whatever the final decision about the role of a given factor (confounder, modifier or explanatory factor), it needs to be justified on the basis of an underlying causal model. If the effects of social class are under study, it is noteworthy that race is liable to affect social class, whereas social class will not affect race. However, if there is evidence that there are biological differences in the disease that are not accounted for by social factors such as lifestyle or treatment, stratification by race may be the preferable option. In general, if a factor is part of the causal chain of events between the exposure and outcome variables, adjustment for it leads to overadjustment and dilution of the real effect. If, for example, place of residence is determined to some extent by social class, one should not adjust for place of residence in a study exploring social class effects.

Causal explanations

General explanation - mortality from other causes The crude (observed) survival rate reflects the mortality from all causes of death. Not all cancer patients die of the cancer they have and intensity of mortality from other causes affects the proportion of cancer deaths; for example, the proportion of deaths from other causes is large in studies of cancer patients in very old age (over 80 years of age). The social class differences in observed survival may, therefore, be due to variation in mortality from other causes of death (Linden, 1969). A great deal of evidence on social class differences in overall mortality has been gathered (see, for example: Antonovsky, 1967; Townsend & Davidson, 1982; Marmot et al., 1984; Fox et al., 1985). Also, mortality from specific causes of death other than cancer is well documented (Fox & Goldblatt, 1982; Davey Smith et al., 1990; Valkonen et al., 1993). In most cancer types, however, mortality from cancer is far more important than mortality from other causes of death. The exceptions may be cancers with low case fatality - for example, squamous cell cancer of the skin. Also, the excess mortality tends to wear off among cancer patients surviving a long time period.

In studies mainly concerned with social class differences in the extraneous mortality due to cancer, survival rates corrected for mortality from other causes of death should be used. These can be obtained by using information on actual causes of death (Dorn, 1950; Parkin & Hakulinen, 1991). An alternative way is to calculate relative survival rates and use social-class-specific expected survival rates (Linden, 1969). The use of general life tables in the calculation of relative survival rates leads to overestimation of the social class differences in cancer-specific mortality. The expected survival rate is too high for lower social classes and, thus, the relative survival rate becomes too low, overestimating the cancer-specific mortality. The opposite is true for the survival rates of higher social classes. This is especially important when the proportion of deaths from other causes is large - that is, in cancers with good prognosis, among older patients and with long follow-up. However, use of corrected survival rates has been an exception rather than rule in studies of social class differences in cancer patient survival; corrected rates have been employed in only a small number of studies (Berg et al., 1977; Bonett et al., 1984; Karjalainen & Pukkala, 1990; Auvinen, 1992).

The contribution of other causes of death was thoroughly evaluated by Berg *et al.* (1977). They estimated that depending on the type of cancer, 25–50% of the survival difference between the indigent and private patients in their study was due to deaths from causes other than cancer. Also, in the studies by Kogevinas (1990) and Auvinen *et al.* (1995), a social class gradient among cancer patients has been observed in deaths from cancer as well as from other causes.

The validity of corrected survival rates depends on the assumption that there are no major social class differences in accuracy of death certificates. This assumption has not, however, been empirically confirmed. Only one study on the subject has been published (Samphier *et al.*, 1988), and this suggests differences in the accuracy of death certificates. If all death certificates were based on pathological diagnoses the social class gradient in cancer mortality would be slightly steeper. A smaller proportion of microscopically confirmed diagnosis among lower social classes has also been reported elsewhere (Auvinen *et al.*, 1995).

Thus, while it is true that the use of observed survival rates leads to overestimation of the social class differences, it is probable that the use of corrected survival rates affects the results in the opposite direction – that is, underestimates them. In theory, the true estimates could be obtained by calculating relative survival rates by using social-class-specific expected mortality rates. This would allow control for other causes of death without assuming similar accuracy of death certificates. Unfortunately, social-class-specific mortality data required for this method are not widely available.

It is our view that the choice of survival measure may not be of crucial importance after all. Relative or observed rates have been compared in some studies. In the study by Karjalainen and Pukkala (1990), the differences in results obtained by using relative or corrected rates were small in ages 25–54 years, but increased in older ages. Auvinen *et al.* (1995) observed slightly larger social class differences when using observed rates compared with corrected rates and concluded that the difference was probably due to overestimation of the differences by observed rates.

An issue related to measurement of survival is the eligibility of cases diagnosed at autopsy. There is some evidence that diagnosis at autopsy is more common in lower social classes and that in the majority of these cases cancer is the underlying cause of death (Auvinen *et al.*, 1995). This suggests that cases first diagnosed at autopsy (at least those with cancer as a cause of death) should be included in the material with zero survival. The obvious justification for this is the fact that the probability of autopsy diagnosis may be determined by social class (through health behaviour).

Specific explanatory factors

To contribute to the prevention of poorer cancer survival in lower social classes, studies of social class differences in cancer survival should explore the etiology of the differences instead of merely describing them. In principle, all prognostic factors need to be considered as potential explanatory factors in the social class differences. This means that, ideally, information on several characteristics of both patient and tumour should be collected. This approach was pioneered by Berg et al. (1977), who was already attempting to quantify the individual contributions of different factors in the 1970s. Because stage of disease at diagnosis and mode of treatment are the principal determinants of outcome in most cancers, they are the most plausible explanatory candidates.

Stage Stage at diagnosis has been suggested as an explanation in most studies discussing the social class differences in cancer patient survival. Information on stage at diagnosis is available and has been analysed in a number of studies. Stage at diagnosis has been shown to be the most important factor contributing to social class differences in cancer patient survival. Nevertheless the importance of stage seems to vary by type of tumour and by country. An association between social class and stage of cancer at diagnosis has also been reported in studies not addressing survival differences (Mandelblatt *et al.*, 1991; Richardson *et al.*, 1992; Wells & Horm, 1992).

The evaluation of the role of stage at diagnosis presented here is superficial out of necessity. A detailed analysis of findings of the early studies is not feasible, primarily due to incomplete reporting of the studies. In many instances, only statistical significance has been reported and not the parameter estimates. It has also been common to present only the results of the univariate analysis and of the final model with all the significant parameters. This makes it impossible to assess the individual effects of the prognostic factors on social class differences.

There are also other considerations that complicate an evaluation of the contribution of stage at diagnosis to social class differences in cancer survival. First, cancer is not a uniform disease entity and there are differences in staging systems and the prognostic impact of stage by primary site. Second, differences in staging systems exist for some primary sites; for example, both Dukes' and TNM staging are currently used in cancers of the colon and rectum. Third, accuracy of staging information varies between studies. The varying degree of misclassification that results from this also makes direct comparison of results difficult. In addition, it is possible that some of the social class differences in survival among patients with the same stage of disease at diagnosis could be due to more accurate staging in the higher social classes. If, say, micrometastases in regional lymph nodes are detected with greater probability in higher social classes than in other groups, this would lead to apparently improved prognosis in this group for patients classified as having local-stage disease as well as for those with regional-stage disease. This artefact is due to the differential accuracy of staging known

as the Will Rogers phenomenon (Feinstein *et al.,* 1985; Greenberg *et al.,* 1991).

In a number of studies, the social class differences observed in the univariate analysis have persisted even after controlling for stage (by stratification or modelling) (Table 1). This has been reported consistently in cancers of the uterine corpus, prostate and bladder. Most studies suggest a similar social class effect that is independent of stage in stomach, lung, kidney and both melanocytic and non-melanocytic skin cancer. Also quite consistently, social class differences have not been detectable after controlling for stage in cancers of the pancreas and ovary, which suggests that stage accounts for most or all of the social class differences in survival of cancer at these primary sites. Results regarding the role of stage are conflicting in breast, colorectal and cervical cancers.

In a study by Chirikos *et al.* (1984), adjustment for age, stage and primary site accounted for a quarter of the differences in survival between patients with white-collar occupations and those with bluecollar occupations, but the differences were no longer statistically significant after the adjustment. A similar pattern was observed when income was used as an indicator of socioeconomic status.

In cancer of the uterine corpus, Steinhorn *et al.* (1986) showed that stage of disease accounted for most of the survival differences between patients from areas with lower mean income and smaller proportion of high-school graduates. The differences remained statistically significant, however. This was not the case for uterine sarcoma, as the gradient between educational groups was steeper after adjustment for the above mentioned factors. Income was not a significant prognostic factor in sarcomas.

In a study of lung cancer, the differences in risk of poor outcome at first year of follow-up between patients with low and high levels of education disappeared after adjustment for sex, comorbidity, histology and stage at diagnosis (Stavraky *et al.*, 1987). Unfortunately, the individual contributions of each of these attributes on differences between educational groups were not reported. Karjalainen and Pukkala (1990) reported larger social class differences in non-localized than in localized stages of breast cancer using both relative and corrected five-year survival rates. Introduction of stage in the multivariate model accounted for a minor part of the social class differences.

Table 1. Differences in stage of cancer at diagnosis by socioeconomic status of patients, and the effect of these differences in cancer patient survival differentials

Reference; country	Proportion of local cases	Method of adjustment	Main results	Comments
Oesophageal cancer Linden, 1969; USA	Not reported	Stratification	Differences equally small within local stage and overall	Relative five-year survival rates
Stomach cancer Linden, 1969; USA	Not reported	Stratification	Large differences within local stage among men and women	Relative five-year survival rates
Lipworth <i>et al</i> ., 1970; USA	<5000 US\$ 4% >5000 US\$ 9%	Rates standardized by proportion of local cases	Small effect among men; adjustment not feasible among women	Observed three-year survival rates; no simultaneous adjustment for age
Lipworth <i>et al</i> ., 1972; USA	Non-private 16% Private 15%	Rates standardized by proportion of local cases	Social class differences pronounced after adjustment	Observed ten-month survival rates; unadjusted results not presented
Kato <i>et al</i> ., 1992; Japan	Non-employed 29% Service 34% Production 32% Clerical 44% Professional 46%	Stratification and regression modelling	Social class differences confined to local stage; differences remained significant after adjustment for stage	Observed five-year survival rates; simultaneous adjustment for age, marital status and urbanity
Colon cancer Lipworth <i>et al.</i> , 1970; USA	<5000 US\$ 9% >5000 US\$ 10%	Standardization by proportion of local cases	Small differences among men, unaffected by ad- justment; among women, high income associated with lower survival rate overall and after adjust- ment	Relative three-year survival rates; no simultaneous adjustment for age
Lipworth <i>et al</i> ., 1972; USA	Non-private 34% Private 30%	Standardization by proportion of local cases	Survival advantage for private patients among men and women after adjustment for stage	Transverse colon. Observed ten-month survival rates; unadjusted results not presented; no simultaneous adjustment for age
Berg <i>et al.</i> , 1977; USA	Indigent 35% Non-indigent 37%	Standardization by proportion of local cases	Differences between indigent, clinic pay and private patients diminished but did not disappear after adjustment for stage	Corrected five-year survival rates; no simultaneous adjustment for age

 Table 1. (contd) Differences in stage of cancer at diagnosis by socioeconomic status of patients and the effect of these differences in cancer patient survival differentials

Reference; country	Proportion of local cases	Method of adjustment	Main results	Comments
Colon cancer Wegner <i>et al.</i> , 1982; USA	Not reported	Regression modelling	A non-significant trend by socioeconomic status after adjustment for stage; unadjusted results not presented	Colorectal cancer. Observed seven-year survival rates; simultaneous adjustment for race, age and sex
Keirn & Metter, 1985; USA	Indigent 34% Non-indigent 29%	Stratification	No significant differences between indigent and non-indigent patients withi stage; unadjusted results not presented	Colorectal cancer. Mediar observed survival time n
Dayal <i>et al</i> ., 1987; USA	Low 34% Medium 42% High 44%	Regression modelling	No clear differences by socioeconomic status after adjustment for stage in colon cancer; unadjusted results not presented	Colon and rectal cancer. Observed survival time; simultaneous adjustment for age and sex
Brenner <i>et al.</i> , 1991; Germany	Low 54% Medium 58% High 51% (colorecta	Stratification	The lowest social class had poorest survival within all stages	Colorectal cancer. Observed survival time and ten-year survival rates
Kato <i>et al</i> ., 1992; Japan	Non-employed 33% Service 36% Production 42% Clerical 46% Professional 38%	Stratification and modelling	Some indication of social class differences within regional stage; overall differences no longer significant after adjustment for stage	Colorectal cancer. Observed five-year survival rates; simultaneous adjustment for age, marital status and urbanity
Auvinen, 1992; Finland	Class I (high) 44% Class II 41% Class III 42% Class IV (low) 37%	Regression modelling	Stage accounted for half of the social class differences	Corrected five-year survival rates; adjusted for age
Rectal cancer Lipworth <i>et al.,</i> 1970; USA	<5000 US\$ 9% >5000 US\$ 16%	Standardization by proportion of local cases	Among men, modest differences unaffected by adjustment; among women, clear differences increased by adjustment	Relative three-year survival rates; no simultaneous adjustment for age
Lipworth <i>et al.,</i> 1972; USA	Non-private 53% Private 36%	Standardization by proportion of local cases	Clear survival advantage for private patients over non-private after adjustment for stage	Observed ten-month survival rates; no simultaneous adjustment for age

Table 1. (contd) Differences in stage of cancer at diagnosis by socioeconomic status of patients and the effect of these differences in cancer patient survival differentials

age

Reference; country	Proportion of local cases	Method of adjustment	Main results	Comments
Rectal cancer Dayal <i>et al</i> ., 1987; USA	Low 34% Medium 42% High 44%	Regression modelling	A non-significant trend by socioeconomic status after adjustment for stage; unadjusted results not presented	Observed survival time; simultaneous adjustment for age, sex and race
Brenner <i>et al.</i> , 1991; Germany	Low 54% Medium 58% High 51% (colorect	Stratification al)	Differences equally large in all stages	Colorectal cancer; results not presented separately for rectal cancer. Ten-year survival rates
Pancreas cancer Linden, 1969; USA	Not reported	Stratification	Differences observed within local stage	Relative five-year survival rates
Larynx cancer Linden, 1969; USA	Not reported	Stratification	Large difference within local stage	Relative five-year survival rates
Berg <i>et al</i> ., 1977; USA	Not reported	Standardization by proportion of local cases	Differences slightly reduced by adjustment for stage	Corrected five-year survival rates
Lung cancer Linden, 1969;	Not reported	Stratification	Marked differences within	Relative five-year survival
USA	Not reported	Stratification	local stage among men	rates
Lipworth <i>et al</i> ., 1970; USA	<5000 US\$ 2% >5000 US\$ 8%	Standardization by proportion of local cases	No clear differences overall nor within stage	Relative three-year survival rates; simultaneous stratification by sex, but not by age
Lipworth <i>et al</i> ., 1972; USA	Non-private 13% Private 24%	Standardization by proportion of local cases	More favourable survival for private than non-private patients among men, but not among women	Observed ten-month survival rates; no simultaneous adjustment for age
Berg <i>et al.</i> , 1977; USA	Indigent 15% Non-indigent 19%	Standardization by proportion of local cases	Modest overall differences disappeared after adjustment for stage	Median corrected survival time; no simultaneous adjustment for age
Keirn & Metter, 1985; USA	Indigent 34% Non-indigent 29%	Stratification	Non-significantly more favourable survival for non-indigent than indigent patients within local and regional stage	Median and 75th percentile of observed survival time; unadjusted survival data not presented by economic status; no adjustment for

Table 1. (contd) Differences in stage of cancer at diagnosis by socioeconomic status ofpatients and the effect of these differences in cancer patient survival differentials

Reference; country	Proportion of local cases	Method of adjustment	Main results	Comments
Lung cancer Stavraky <i>et al.</i> , 1987; Canada	Not reported	Regression modelling	Modest overall differences by education disappeared after adjustment for stage	Odds ratio of death at one year of follow-up; simultaneous adjustment for age, sex, histology, employment status and comorbidity
Breast cancer in women Linden, 1969; USA	County 82% Private 83%	Statification (local versus all)	Differences between county and private hospital patients smaller within local stage than among all patients	Relative ten-year survival rates; age group 55–64 years
Lipworth <i>et al.</i> , 1972; USA	Non-private 31% Private 40%	Standardization by proportion of local cases	More favourable survival among private patients compared with nonprivate after adjustment for stage	Observed 10-month survival rate; no simultaneous adjustment. for age; unadjusted rates not provided
Berg <i>et al</i> ., 1977; USA	Indigent 35% Non-indigent 38%	Standardization by proportion of local cases	Differences between indigent, clinic pay and private patients diminished but did not disappear after adjustment for stage	Corrected five-year survival rates
Dayal <i>et al</i> ., 1982; USA	Not reported	Regression modelling	Social class differences remained significant after adjustment for stage; point estimates not reported	Observed survival time; no simultaneous adjustment for age
Keirn & Metter, 1985; USA	Indigent 45% Non-indigent 35%	Stratification	Non-significantly more favourable survival for non-indigent than indigent patients within local and regional stage	Median, 75th and 80th percentile of observed survival time; unadjusted survival data not presented by economic status; no adjustment for age
Bassett & Krieger, 1986; USA	Not reported	Regression modelling	Statistically significant differences after adjustment for stage	Observed survival time; adjustment for age, race and histological type
Karjalainen & Pukkala, 1991; Finland	Class I (high) 51% Class II 51% Class III 48% Class IV (low) 47%	Stratification and modelling	Differences apparent mainly within nonlocal stage and remained significant after adjustment for stage	Corrected and relative five-year survival rates; simultaneous adjustment for age and year of diagnosis

Table 1. (contd) Differences in stage of cancer at diagnosis by socioeconomic status of patients and the effect of these differences in cancer patient survival differentials

Reference; country	Proportion of local cases	Method of adjustment	Main results	Comments
Breast cancer in women Gordon <i>et al.</i> , 1992; USA	Not reported	Regression modelling	Differences remained significant after adjustment for tumour diameter and number of positive lymph nodes	Observed and disease- free survival time; adjustment for race and estrogen receptors
Cancer of the uterine ce	rvix			
Linden, 1969; USA	Not reported	Stratification	No differences within local stage	Five-year cumulative survival rate
Lipworth <i>et al</i> ., 1970; USA	<5000 US\$ 35% >5000 US\$ 45%	Standardization by proportion of local cases	Differences decreased slightly but did not disappear after adjustment for stage	Three-year relative survival rate; no simultaneous adjustment for age
Lipworth <i>et al</i> ., 1972; USA	Non-private 38% Private 35%	Standardization by proportion of local cases	Survival advantage for private patients compared with non-private after adjustment for stage	Ten-month survival rates; unadjusted rates not presented; no simultaneous adjustment for age
Berg <i>et al.</i> , 1977; USA	Indigent 69% Non-indigent 75%	Standardization by proportion of local cases	Differences between indigent, clinic pay and private patients diminished but did not disappear after adjustment for stage	Five-year corrected survival rates; no simultaneous adjustment for age
Cancer of the uterine con	rpus			
Linden, 1969; USA	Not reported	Stratification	Differences observed also within local stage	Relative five-year survival rate
Lipworth <i>et al</i> ., 1970; USA	<5000 US\$ 35% >5000 US\$ 46%	Standardization by proportion of local cases	No differences overall nor after adjustment for stage	Relative three-year survival rates
Lipworth <i>et al</i> ., 1972; USA	Non-private 48% Private 60%	Standardization by stage distribution	More favourable survival for private than non-private patients after adjustment for stage	Observed 10-month survival rates; unadjusted rates not presented; no simultaneous adjustment for age
Berg <i>et al.</i> , 1977; USA	Not reported	Standardization by stage distribution	More favourable survival for non-indigent than indigent patients after adjustment for stage	Corrected five-year survival rates; unadjusted corrected rates not presented; adjusted for age

 Table 1. (contd) Differences in stage of cancer at diagnosis by socioeconomic status of patients and the effect of these differences in cancer patient survival differentials

Reference; country	Proportion of local cases	Method of adjustment	Main results	Comments
Cancer of the uterine c	orbus		· · · · · · · · · · · · · · · · · · ·	······································
Steinhorn <i>et al.</i> , 1986; USA	Not reported	Regression modelling	Stage accounted for most of the differences, but they remained statistically significant also after adjustment for stage. For uterine sarcoma the differences between educational groups were larger after adjustment for stage	Observed survival time and five-year rates; simultaneous adjustment for age, race and area
Cancer of the ovary				
Linden, 1969; USA	Local only	Blocking	No differences within local stage	Relative five-year survival rates
Lipworth <i>et al.</i> , 1970; USA	Non-private 27% Private 21%	Standardization by proportion of local cases	No differences after adjustment for stage	Observed ten-month survival rates
Lipworth <i>et al.</i> , 1972; USA	Non-private 13% Private 30%	Standardization by proportion of local cases	No differences overall nor after adjustment for stage	Relative three-year survival rates
Kidney cancer Linden, 1969; USA	Not reported	Stratification	Differences observed within local stage	Relative five-year survival rates
Bladder cancer				
Linden, 1969; USA	Local only	Blocking	Clear differences observed within local stage among both sexes, although not as large as the overall differences	Relative five-year survival rates
Lipworth <i>et al.</i> , 1970; USA	<5000 US\$ 39% >5000 US\$ 36%	Standardization by proportion of local cases	Adjusted differences larger than unadjusted among men; direction of differences reversed after adjustment among women	Relative three-year survival rates; no simultaneous adjustment for age
Lipworth <i>et al.</i> , 1972; USA	Non-private 66% Private 63%	Standardization by proportion of local cases	Clear differences after adjustment for stage among men and women	Observed ten-month survival rates
Berg <i>et al</i> ., 1977; USA	Indigent 70% Non-indigent 75%	Standardization by proportion of local cases	Differences reduced only slightly by adjustment for stage	Corrected five-year survival rates; no simultaneous adjustment for age

Table 1. (contd) Differences in stage of cancer at diagnosis by socioeconomic status of patients and the effect of these differences in cancer patient survival differentials

Reference; country	e; country Proportion of Method of Main results local cases adjustment		Comments		
Prostate cancer Lipworth <i>et al.</i> , 1970; USA	<5000 US\$ 27% >5000 US\$ 16%	Standardization by proportion of local cases	Differences remained equally large after adjustment for stage	Relative three-year survival rates	
Lipworth <i>et al.</i> , 1972; USA	Non-private 57% Private 52%	Standardization by proportion of local cases	Differences observed after adjustment for stage	Observed ten-month survival rates	
Berg <i>et al.</i> , 1977; USA	Indigent 49% Non-indigent 44%	Standardization by proportion of local cases	Differences almost equally large after adjustment for stage	Observed seven-year survival rates; no adjustment for age	
Dayal <i>et al.</i> , 1985; USA	Not reported	Regression modelling	Differences observed in all stages	Observed survival time; adjusted for age; stage-adjusted point estimates not reported	
Clark & Thompson, 1994; USA	Enlisted 75% Officers 80% (clinical stage)	Stratification	No differences overall or within stage	Observed five-year survival rates; no adjustment for age	
Melanoma of the skin Linden, 1969; USA	Not reported	Stratification	Analysis by stage not feasible because of small numbers of cases	Corrected five-year survival rates	
Berg <i>et al.</i> , 1977; USA	Not reported	Standardization by proportion of local cases	Differences almost disappeared after adjustment for stage	Corrected five-year survival rates	
Shaw <i>et al</i> ., 1981; Australia	Stage I only	Blocking	Differences considerably smaller, yet significant within stage I	Observed five-year survival rates	
Skin cancer (excluding	melanoma)				
Linden, 1969; USA	Not reported	Stratification	Differences within local stage as large as overall differences	Relative five-year survival rates	
Berg <i>et al.,</i> 1977; USA	Indigent 96% Non-indigent 95%	Standardization by stage distribution	Adjustment for stage did not alter the differences	Observed, relative and corrected five-year survival rates; differences mostly due to other causes of	

death

Brenner *et al.* (1991) observed poorer survival for colorectal cancer patients of low social class than for patients of middle or high social class in local, regional and distant stages. The difference in fiveyear observed survival rate between the lowest and highest social class was between 5 and 10% in all stages.

In a study of breast cancer patients by Gordon *et al.* (1992) adjustment for stage did not materially diminish the socioeconomic differences. In the analysis of disease-free survival, the excess risk of death associated with residence in an area with low education diminished only slightly after adjustment for number of positive axillary lymph nodes, tumour diameter and estrogen receptor status. Similar results were obtained in the analysis of overall survival. In a study of colon cancer conducted in Finland, introduction of stage in the model explained half of the social class differences (Auvinen, 1992). After the adjustment, the social class differences were no longer statistically significant.

In a Japanese study with almost 4500 cancer patients, most favourable survival was observed in the highest occupational class (professional and managerial). The trend by occupational class was no longer significant after adjustment for stage in gastric cancer and in colorectal cancer (Kato *et al.*, 1992). In a study conducted in France, the effect of socioeconomic status (assessed on the basis of housing) was studied among 771 colorectal cancer patients (Monnet *et al.*, 1993). There were statistically significant differences in survival by socioeconomic status among patients with localized disease, but not among patients with advanced disease.

It should be noted that stage is in turn determined by a number of other factors related to both tumour and host. In fact, stage is sometimes regarded as an expression rather than as a determinant of prognosis *per se*. These factors are discussed under 'Determinants of stage and treatment'.

Treatment Outcome of treatment depends on the treatment modality, quality of treatment, and characteristics of the tumour and the patient. To avoid confusion, these should be addressed separately. Most of the research in the field has concentrated on the choice of treatment, which is obviously based on feasibility. As concerns equity, it is important to know whether social class differences in

survival are due to differences in access to treatment or in the quality of treatment.

Choice of treatment. Choice of treatment modality is a matter of critical importance in the outcome of cancer. In many cases, there are treatment protocols depending on, for example, primary site, histological type and stage of the tumour, as well as on age and health status of the patient. Differences in choice of treatment have been reported depending on insurance coverage and marital status (Greenberg *et al.*, 1988) as well as on urbanity (Howe *et al.*, 1992; Launoy *et al.*, 1992). In countries where the patient is responsible for a substantial part of the cost of treatment, economic factors may also be important in the feasibility of some costly treatments.

The potential contribution of treatment to the occurrence of social class differences in cancer patient survival was first directly assessed by Linden (1969) and Lipworth *et al.* (1970, 1972), but the effect of treatment has been directly addressed in only a small number of subsequent studies (Table 2). The findings of some studies indicate that social class differences in treatment have contributed to survival differences.

Linden (1969) stratified his material of 1662 breast cancer patients by age, race, stage and treatment. The social class differences in survival were equally large among breast cancer patients with surgically treated localized tumours as in the whole material. In the first study by Lipworth et al. (1970), the proportion of patients receiving neither surgery nor radiotherapy was larger among patients residing in a low-income area than among those residing in a high-income area in bladder cancer among both sexes and in rectal cancer among men, but there was a reverse association in cancers of the stomach and colon, and among women with rectal or lung cancer. Statistical significance of the differences was not assessed. The authors concluded that the social class differences in the assignment of treatment cannot explain the differences in survival. In another study, Lipworth et al. (1972) analysed patients with localized or regional stage combining several primary sites (standardizing the survival rates on the site). The proportion of patients dying within four months was higher among non-private than private patients in all age and treatment strata.

Berg *et al.* (1977) found differences in survival from several types of cancer between two groups defined by socioeconomic status, although the

389

patients were treated by the same staff and should have received equal treatment. Opposite results have also been obtained. Page and Kuntz (1980) studied survival among Veterans Administration male cancer patients, and found no differences in survival by race or income except in bladder cancer. They concluded that the lack of differences was due to the fact that all the patients they studied received the same treatment with no distinctions, whereas most American hospitals placed their patients into categories on the basis of ability to pay.

In childhood leukaemia, no social class differ-

ences in treatment modality were detected by McWhirter *et al.* (1983). Keirn and Metter (1985) found that there were no differences in survival by economic status among lung, breast and colorectal cancer patients treated in a hospital that accepted patients regardless of race or ability to pay. Dayal and Chiu (1982) noted that the lack of a significant racial difference in the Veterans Administration study (Page & Kuntz, 1980) may have been due to the selective nature of the patient population. The income level of both Blacks and Whites who used the Veterans Administration hospital was relatively

Tab	le 2. Treatmen	it and social class	eonerendide:	s in cancer patient s	Burvival
Reference	Primary site	Treatment distribution	Method of analysis	Main results	Comments
Linden, 1969; USA	Breast	Surgical treatment for 82% of county hospital and 83% of private hospital patients	Blocking	Differences observed also among surgically treated patients	Relative and corrected 10-year survival rates; local stage only
Lipworth <i>et al</i> ., 1972; USA	Several sites combined	No surgery or radiotherapy for 7% of private and 21% of non-private patient with locoregional disease	Blocking	Differences observed within both treatment groups	Observed 20-day survival rate
Chirikos <i>et al.,</i> 1984; USA	Several sites combined	Surgery versus radio/chemotherapy without surgery versus others – distribution not reported	Regression modelling	Differences diminished and no longer significant after adjustment for treatment	Observed survival time; simultaneous adjustment for 'severity'
Chirikos & Horner, 1985; USA	Digestive tract, colorectal	Surgery for 42% of high-income, 40% of middle-income and 41% of low-income patients in colorectal cancer	Regression modelling	Differences persist after adjustment for treatment	Observed survival time; simultaneous adjustment for age and stage
Auvinen, 1992; ⁻ inland	Colon	Curative surgery for 54% of patients in social class I, 53% in classes II and III, and 44% in class IV (lowest)	Regression modelling	Treatment accounted for the remaining differences after adjustment for stage	Corrected five-year survival rates; simultaneous adjustment for stage

low. Therefore the study population may have been too homogeneous with respect to socioeconomic status. The same criticism might be applied to the study of Keirn and Metter (1985).

McWhorter and Mayer (1987) studied the association between race and type of initial treatment in 1978–1982 in the USA and found that Blacks received less radical treatment. Black patients also had lower survival rates. In the study by Chirikos et al. (1984), social class differences were no longer significant after adjustment for age, stage and primary site. Further adjustment for treatment did not have an effect on the point estimate nor significance. In the small sample of Chirikos and Horner (1985), social class differences in survival between colorectal cancer patients with high and low income remained statistically significant even after adjustment for both stage and surgical treatment. In the study of colon cancer patients by Auvinen (1992), all social class differences in the risk of cancer death were diminished by adjustment for stage and disappeared after further adjustment for surgical treatment.

Choice of treatment may also depend on tumour characteristics, such as histology, and on host factors, such as age or comorbidity. These are discussed under 'Determinants of stage and treatment'.

Quality of treatment. It has been suggested that even when patients are given the same type of treatment, there may be 'differences in treatment efficacy' by social class (Vågerö & Persson, 1987). Quality of treatment received may vary between hospitals. The fact that social class differences have tended to be smaller in studies based on one hospital only than in studies covering several treatment centres (Weston et al., 1987 versus Savage et al., 1984 in myeloma; Berg et al., 1977 versus Linden, 1969 in stomach and oesophagus cancer and leukaemia: Keirn & Metter, 1985 versus Linden, 1969 in lung, breast and colorectal cancers; Chirikos & Horner, 1985 versus Dayal et al., 1987 in colorectal cancer) also provides some support for the role of treating hospital. It is, however, also possible that the socioeconomic background of the patients is similar within the single hospitals and the differences are not observed because of a narrow spectrum of socioeconomic status rather than uniform treatment.

Choice and implementation of treatment are also affected by compliance/patient involvement. It may

be easier for patients from higher social classes to communicate with doctors (Epstein *et al.*, 1985), which may affect choice of treatment, compliance and followup. Also, a direct effect of social class on quality of care has been suggested in a study by Burstin *et al.* (1992), who reported greater risk of medical injury due to substandard care among uninsured patients.

Access to and quality of treatment seem to be associated with place of residence (West & Lowe, 1976; Stiller, 1988), which is, in turn, associated with social class. Geographic area was not a prognostic factor in the multivariate analysis and did not account for the social class differences in cancer of the uterine corpus in the study by Steinhorn *et al.* (1986). Similar results were obtained for cancers of the colon and rectum by Brenner *et al.* (1991). Urban residence has not accounted for the social class differences in colon cancer (Bonett *et al.*, 1984; Brenner *et al.*, 1991; Auvinen, 1992) nor in breast cancer (Bonett *et al.*, 1984).

It is not clear, however, how information on treatment could or should be taken into account in observational survival studies (Hakulinen, 1983). In observational studies, the treatment distribution is influenced not only by treatment practices, but also by stage distribution. As noted by Morrison *et al.* (1976), 'treatment tended to be selected according to apparent prognosis'. This emphasizes the importance of not regarding stage and treatment as 'independent' prognostic factors, but as hierarchical parts of a causal chain.

Determinants of stage and treatment

Tumour characteristics. Different tumour biology is one explanation proposed for the social class gradient in survival (Lipworth et al., 1970; Berg et al., 1977; McWhirter et al., 1983; Chirikos & Horner, 1985). Tumour characteristics possibly associated with response to a given mode of therapy are, in part, the same as those affecting stage of disease at diagnosis. Grade of differentiation is a principal determinant of aggressiveness of a tumour in several primary sites. The probability of achieving a remission by chemotherapy or radiotherapy may depend on growth rate of the tumour or presence or absence of a specific genetic trait, such as the MDR2, p53, or c-erbB2 gene. However, the relatively little information available suggests that biological indicators of tumour aggressiveness are not important determinants of social class differences in cancer survival.

391

It is possible that the characteristics of the tumours differ across social classes as a function of etiological factors and these are reflected in differences in survival. For instance, Ramot and Magrath (1982) have suggested that the increased incidence of childhood leukaemia in higher social classes is mainly due to excess of common acute lymphoblastic leukaemia, which has a better prognosis. However, Dayal and Chiu (1982) are against the hypothesis that there are differences in tumour biology by social class, and claim that the elements of social status influencing etiology are different from those predicting survival. Ewertz et al. (1991) did not find a significant association between survival of breast cancer patients and the most important risk factors for this disease. If the differences in exposure to risk factors led to differences in tumour characteristics (important for prognosis), this would have been detected in this study. Furthermore, tumour aggressiveness is associated with the characteristics of the patients, such as the immune system, which may play a more important role than the tumour factors themselves.

Histological type is associated with aggressiveness of the tumour in a number of cancers. In the study by Bassett and Krieger (1986), adjustment for histology (ductal, lobular or other) did not account for the social class differences in breast cancer survival. In the study of Steinhorn et al. (1986), social class differences in survival from adenocarcinoma of the uterine corpus were of the same magnitude as in uterine sarcomas. No clear social class differences were observed either before or after adjustment for histological type (squamous cell versus others) among lung cancer patients in the study by Stavraky et al. (1987). Auvinen et al. (1995) reported effect modification by cell type in lung cancer and leukaemia among men in their study based on more than 100 000 cancer patients. Social class differences were not observed among all patients, but they were confined to non-small-cell lung cancer and acute leukaemia.

Other tumour characteristics that have been studied in relation to social class differences in cancer patient survival include primary-site-specific prognostic factors such as initial white cell count in childhood leukaemia (McWhirter *et al.*, 1983), serum albumin and haematocrite in myeloma (Savage *et al.*, 1984), hormone receptors in breast cancer (Gordon *et al.*, 1992), tumour thickness in melanoma (Shaw *et al.*, 1981) and grade of differentiation in soft tissue sarcoma (Ciccone *et al.*, 1992). These factors have not accounted for the social class differences in survival. In the study by Savage *et al.* (1984), overcrowding remained the most important determinant of outcome even after adjustment for biological prognostic factors such as tumour burden, serum albumin and haematocrite. Carnon *et al.* (1994) assessed in a recent study the role of tumour size, nodal status, histological grade and estrogen receptor concentration in relation to social class differences in breast cancer survival. None of the biological indicators of prognosis was associated with social class.

Host factors. Host factors include both biological factors, such as presence of other chronic diseases, and psychosocial factors, such as health behaviour before or after diagnosis.

Several host factors are related to stage of disease at diagnosis. The importance of host factors for the occurrence of survival differences has scarcely been studied. Host resistance or host-tumour relationship has frequently been suggested as a mediator of the effect of social class on cancer patient survival. However, the exact meaning of the terms has remained unclear apart from the remarks that host resistance may be influenced by, for example, nutrition and that immunological mechanisms may be involved. Thus it is unclear how they should be operationalized.

Presence of any other chronic disease did not appear an independent prognostic factor in the study by Stavraky *et al.* (1987) and was not used in the multivariate analyses.

Health behaviour affects the diagnosis of a cancer and often does vary between social classes. Differences in health behaviour have been proposed as potential explanatory factors for social class differences in cancer patient survival. An example of a behavioural factor is the delay between first symptom and diagnosis of cancer. This time period depends on how the symptoms are observed and interpreted by the patient, as well as on the pattern of seeking medical attention. The first phase – observation and interpretation of symptoms – is essentially psychological and depends on knowledge and awareness. Hackett *et al.* (1973) have suggested that the longer delay among patients from lower social classes may be due to fear and

denial. Patients who recognized their condition as a possible cancer had a shorter delay in seeking medical advice than those using a more general or vague expression for it. Taking action – that is, making an appointment with a doctor – may depend on economic resources and also on earlier experiences with health care. Longer delay among patients from lower social classes has been reported in breast cancer (Richardson *et al.*, 1992; Vineis *et al.*, 1993), and in colorectal cancer (MacArthur & Smith, 1984).

Host factors commonly interfere with implementation of already chosen treatment through complications caused by, for example, bone marrow, heart or neural toxicity of chemotherapy. There are individual differences in susceptibility to such complications, but their relationship to factors such as specific diseases, general health status and nutritional status, or lifestyle factors such as smoking or alcohol consumption, is not clear.

Psychosocial factors. A direct effect of psychosocial factors in cancer survival has also been suggested but results are contradictory. Furthermore, correlation of the psychosocial factors with social class, not to mention empirical assessment of their contribution to social class differences, has rarely been assessed.

In breast cancer, social network (Waxler-Morrison *et al.*, 1991) and certain traits of personality (Hislop *et al.*, 1987) were associated with favourable survival after controlling for clinical prognostic factors. This could not be confirmed in another study (Cassileth *et al.*, 1988). Similarly, the initial findings on the effects of adverse life events on relapse of breast cancer (Ramirez *et al.*, 1989) have not been supported by subsequent research (Barraclough *et al.*, 1992). It has also been reported that quality of life predicts survival in breast (Coates *et al.*, 1992) and lung cancer (Ganz *et al.*, 1991) as well as melanoma (Coates *et al.*, 1993).

It may nevertheless be worthwhile to consider these factors when searching for reasons for the social class differences in cancer survival. A number of methodological problems remain: the studies have mostly been based on materials with insufficient sample size, instruments used for measurement of psychosocial factors have been diverse and the control for conventional prognostic factors has been inadequate. Not only have the validity and reliability of the studies been different, but also they have also been developed for various purposes. Also, the fact that quality of life scores correlate with survival is not sufficient to prove an independent prognostic effect since adjustment for other prognostic factors has been inadequate in some studies. It is plausible that quality of life is affected by extent of disease and this should be taken into account carefully before accepting a reverse relationship. Studies with intervention to improve quality of life have yielded contrasting results (Spiegel *et al.*, 1989; Gellert *et al.*, 1993).

Final remarks

Social class differences in cancer patient survival have been extensively described in the literature. It seems that cancer is diagnosed at an advanced stage more often in lower than in higher social classes. However, the survival differences by social class have persisted even after adjustment for stage in most studies. In a small number of studies, the contribution of treatment to the survival differences has also been assessed. The results are somewhat contradictory: some of the studies showed social class differences even after controlling for treatment, while in other studies the differences disappeared after adjustment for treatment.

The conflicting results are understandable because there is probably real variation in the extent of the social class differences and in the relative importance of factors among different primary sites and countries. Furthermore, the social class indicator used influences the results, because different indicators measure different dimensions of social stratification and because the relative sizes of each class may vary. Hence, one must be careful in generalizing the results from a single study.

It is apparent, however, that the understanding of the phenomenon is still superficial. In most of the studies, a descriptive approach has been adopted. Thus most of the research has concentrated on simple hypothesis testing (the questions addressed being directed at existence versus non-existence of the phenomenon and the conclusion based on statistical significance) and/or quantification of the effect.

A descriptive approach to research on the subject can hardly yield valuable new information now, at least in the industrialized countries where a number of studies have already demonstrated the extent of

393

the problem. For the development of strategies to diminish the differences, there is an urgent need to understand the etiology of such differences – that is, which factors are involved in the genesis of the differences and what is their relative contribution.

These factors cover several domains: behavioural (values and attitudes of the patient, health behaviour), social (social support, economic resources) and clinical (functional status and comorbidity, choice of treatment, response to treatment, complications, relapse, cause of death). Also, the temporal dimension of these factors ranges from the first symptom to the diagnosis, treatment and the eventual death of the patient. This makes it impossible to obtain information on all relevant aspects from a single source. The relevant set of variables also differs between different types of cancer. The complexity is real – that is, no improvements in, say, measurement of social class or survival can be expected to decrease it.

Some potential approaches for intervention may be outlined already. Even if there is not sufficient proof of their efficacy in decreasing social-class differences in cancer patient survival in lower social classes, their implementation can be justified by benefit for the general population. If the importance of some of them is proven in the future, they could be directed especially to the lower social classes. Health education programmes to increase awareness of early symptoms might improve stage at diagnosis. Screening, if accessible, could have the same effect, although efficacy has not been proven for types of cancer other than cancers of the breast and uterine cervix (for further discussion, see the chapter by Segnan). Furthermore, efforts to diminish economic barriers to utilization of health care services are warranted. One can also consider whether patients from lower social classes should be regarded as a high-risk group and consequently allocated an intensified treatment regime. It is equally plausible, however, that they are more vulnerable to complications of cancer treatment and a conservative line of treatment should be the preferred option.

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