Original article

Changes over time in socioeconomic inequalities in breast and rectal cancer survival in England and Wales over a 32-year period (1973-2004): the potential role of health care

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ABSTRACT

INTRODUCTION: Socioeconomic inequalities in cancer survival are well documented but they differ for different cancers and over time. Reasons for these differences are poorly understood.

PATIENTS AND METHODS: For England and Wales, we examined trends in socio-economic survival inequalities for breast cancer in women and rectal cancer in men during the 32-year period 1973-2004. We used a theoretical framework based on Victora's 'inverse equity' law, under which survival inequalities could change with the advent of successive new treatments, of varying effectiveness, which are disseminated with different speed among patients of different socioeconomic groups. We estimated 5-year relative survival for patients of different deprivation quintiles and examined trends in survival inequalities in light of major treatment innovations.

RESULTS: Inequalities in breast cancer survival (921,611 cases) narrowed steadily during the study (from -10% to -6%). In contrast, inequalities in rectal cancer survival (187,104 cases) widened overall (form -5% to -11%) with fluctuating periods of narrowing inequality.

CONCLUSION: Trends in socioeconomic differences in tumour or patient factors are unlikely explanations of observed changes over time in survival inequalities. The sequential introduction into clinical practice of new treatments of progressively smaller incremental benefit may partly explain the reduction in inequality in breast cancer survival.

Key words: Breast, Cancer, Colorectal, Deprivation, Inequality, Survival, Trends, Socioeconomic.

INTRODUCTION

Wide socioeconomic inequalities in survival have been reported for many cancers.[1,2] Evidence on the causes of these inequalities remains limited, but they may at least partly reflect differences in clinical management (the 'healthcare factors' hypothesis).[1,2] If this hypothesis were correct, socioeconomic inequalities should be largely determined by socio-economic differences in the quality of treatment received, with deprived patients more often managed sub-optimally. Directly examining this hypothesis is difficult, however, because the treatment information routinely collected by cancer registries, at least historically, is usually in the form of binary (yes/no) information about the main treatment modalities (surgery, radiotherapy, chemotherapy) given within six months of diagnosis, with no information on the timeliness and technical excellence of surgery, or the timeliness, nature, dose and sequencing of radiotherapy or chemotherapy regimes.

An alternative approach is to examine long-term trends in survival inequalities to identify whether the 'advent' of major new treatments was followed by narrowing or widening of inequalities in survival. We use the term 'advent' to denote the timing of market authorisation of new drug therapies; or of the introduction into clinical practice of new surgical and radiotherapy techniques, also often associated with peer-reviewed publication of 'key' relevant studies. This approach is inferior to direct examination of the impact of new treatments on survival using individual patient data, but it may provide insights into the interpretation of historical changes in survival inequalities during periods when population-based cancer treatment data were absent or rudimentary.

The 'inverse equity law' is a conceptual framework, proposed by Victora and colleagues,[3] as an extension of Hart's 'inverse care law',[4] within which the advent of

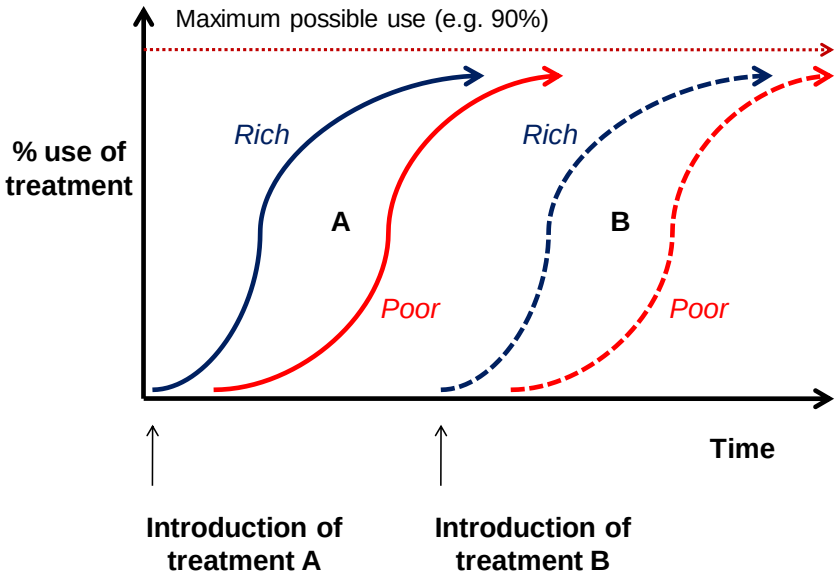
a single new treatment may generate healthcare inequalities that are later resolved. According to this framework, inequality in use of a specific healthcare intervention widens soon after its introduction but later narrows, until it ceases to exist (Figure 1). Evidence exists for time-lagged dissemination of new interventions among lower socioeconomic groups for cervical cancer screening,[5] measles, mumps and rubella (MMR) immunisation,[6] and primary care quality improvements for chronic diseases other than cancer.[7]

Applying Victora's framework to cancer care is challenging, as it typically involves combinations of different treatment modalities (e.g. surgery, chemotherapy or radiotherapy). Step-wise but marginal improvements in survival following introduction of a new drug, for example, may be difficult to detect against underlying trends attributable to refinement and wider dissemination of older treatments, or to improvements in the organisation of services. Testicular cancer provides a rare example of very rapid improvement in survival outcomes soon after the introduction of a single, new and highly effective treatment, platinum-based chemotherapy, in the 1970s.[8] Newer cancer treatments are now introduced into clinical practice frequently, so identifying the treatment(s) responsible for socio-economic inequalities in survival at any point in time may be difficult. Moreover, socio-economic inequalities in access to newer treatments may be arising at the same time that inequalities in the use of more established treatments are being resolved (Figure 1). For these reasons, the evolving causes of inequality in cancer survival, and the likely role of specific healthcare interventions at different times, may be difficult to establish with precision. The relative effectiveness of new *vs.* existing treatments is also relevant. If newer treatments are much more effective than existing ones, inequalities in survival are likely to widen, whereas if newer

treatments are only marginally more effective, then inequalities in outcomes are likely to narrow.

We examined changes in socioeconomic inequalities in survival for breast cancer in women and rectal cancer in men in England and Wales over the 32-year period 1973-2004. We chose these cancers because they are common, and because socioeconomic inequalities in survival became narrower during the 1980s and 1990s for breast cancer, but became wider for rectal cancer.[9,10] We also examined whether any inflection in the underlying survival trends (and socio-economic inequalities) could be linked to the advent of new treatments considered to have been major advances in cancer management during this period.

Figure 1. When an effective new treatment (A) first becomes available, its use is initially higher among more affluent patients. Later, uptake increases among more deprived patients, eventually catching up with levels in affluent groups. Equal use of the treatment is reached after a lag period has elapsed. However the cycle may start again, for another, newer, treatment (B), giving rise to another inequality-equality lag cycle, and perpetuating socio-economic inequalities in healthcare.



METHODS

Two cancer specialists with extensive experience in the management of cancers of the breast (MB) and rectum (MRT) summarised the most important developments in the clinical management of breast and rectal cancers since 1971, and provided insight into the timing of their introduction to cancer management in the UK. This information was provided without knowledge of the findings of the study.

*C*ancer registrations were available from the Office for National Statistics for residents of England and Wales diagnosed with breast or rectal cancer during the 36-year period 1971-2006 and followed up to 31 December 2007. Patients were assigned to one of five categories of socioeconomic deprivation (1 most affluent; 5 most deprived) using area-based measures. The Carstairs deprivation index score of the Census Enumeration District of residence was used for patients diagnosed during 1971-1995 (relating to the 1981 and 1991 Censuses for patients diagnosed 1971-1985 and 1986-1995, respectively).[11] The Index of Multiple Deprivation (IMD) 2004 score of the Lower Super-Output Area of residence was used for patients diagnosed during 1996-2006 (2001 Census).[12] Use of these different deprivation indices has been shown not to introduce bias in relation to relative survival deprivation estimates.[13,14]

Relative survival up to five years after diagnosis was estimated for each calendar year of diagnosis 1971-2006 and each deprivation group, with a STATA algorithm,[8] (http://www.lshtm.ac.uk/ncdeu/cancersurvival/tools/index.htm) adapting methods developed by Esteve and colleagues.[15] Relative survival estimates the cancer-related survival, adjusting for background mortality in the general population. For England and Wales separately, the background mortality was provided by complete (single-year-of-

age) life tables by sex, calendar year and deprivation category. For 2006 and 2007, the 2005 life tables were used because relevant mortality data were unavailable. The cohort approach was used for 5-year relative survival for patients diagnosed during 1971-2002, since at least 5 years' follow-up was available for all patients. For patients diagnosed during 2003-2006, short-term predictions of survival were made with the period approach,[16] and with the hybrid approach for patients diagnosed in 2007.[17] Stratification by year of diagnosis (32 years) and deprivation (5 categories) produced 160 strata, and even with these very common cancers, the precision of year-on-year survival estimates was reduced, so trends were smoothed with five-year moving averages.

We estimated trends in relative survival at one year and five years after diagnosis, and at five years conditional upon one-year survival, for each deprivation group. For brevity, only the plots of five-year survival for the least and most deprived groups are presented in the article. Absolute deprivation gaps in five-year survival were calculated as the simple differences between the fitted survival estimates for the most and the least deprived groups derived from a linear regression model. These were displayed graphically and inspected for temporal change in survival inequalities.

RESULTS

Data for 921,611 women with breast cancer and 187,104 men with rectal cancer diagnosed during the period 1971-2006 were included in the analyses.

For women with breast cancer, five-year relative survival improved steadily from 55% to 85% between 1973 and 2004. Survival improved in each deprivation group, and the deprivation gap in survival has narrowed gradually over most of the 32-year period (from -10% to nearly -6%), except for two brief periods in the early 1980s and early 1990s, during which it was more stable (Figure 2).

During the study period, adjuvant chemotherapy had been shown to be effective originally in 1976 and with an increasingly supportive evidence basis thereafter during the 1980's.[18,19] Similarly, endocrine therapy had been shown to be effective during the 1980's,[18] with evidence also emerging from UK trials.[20,21] The UK breast cancer screening programme was introduced gradually from 1988 to 1993.[22]

Five-year relative survival for men with rectal cancer improved from 29% to 53% between 1973 and 2004 (Figure 3). Survival increased in each deprivation group, but not at the same pace, and the survival deficit has widened from -5% to -11% since the 1970s. Two distinct 'cycles' can be seen. The deprivation gap in survival narrowed slightly in the late 1970s but then widened even more by the mid-1980s; a second 'cycle' of this type occurred between the late 1980s and the early 1990s, and the deprivation gap has remained greater than -10% since the late 1990s.

Effective interventions for rectal cancer introduced during the study period included increasing use of flexible sigmoidoscopy since the 1970s; improvements in the quality of surgery because of specialisation since the early 1990s and thereafter (also resulting in decreasing post-operative mortality);[23,24,25] introduction of 'Total Mesorectal Excision', first described in 1986,[26] and further developed and disseminated throughout the 1990s;[27] more frequent use of pre-operative radiotherapy, with conclusive evidence of efficacy since 2000,[28] and more frequent use of adjuvant chemotherapy.[29,30] Increasing use of liver resection surgery to manage metastatic disease in patients who present with operable liver involvement was apparent in late 1990s and beyond.[31]

Figure 2. Trends in 5-year relative survival (%) from breast cancer in women in the most affluent and most deprived groups, and deprivation gap (%) in survival: 5-year moving average values, England and Wales, 1973-2004. Periods of emergence of evidence about the efficacy of new interventions are denoted on the graph.

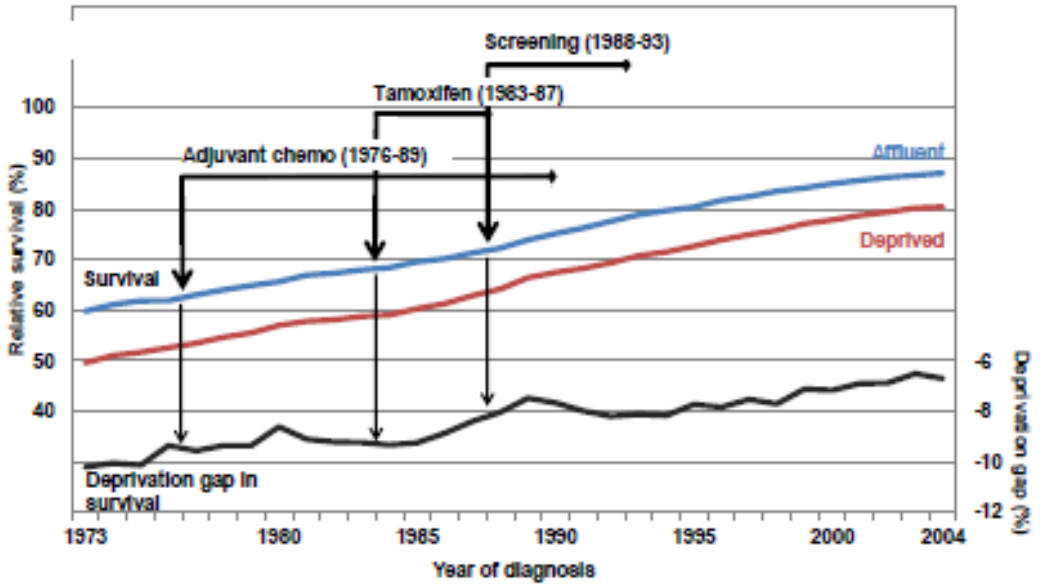
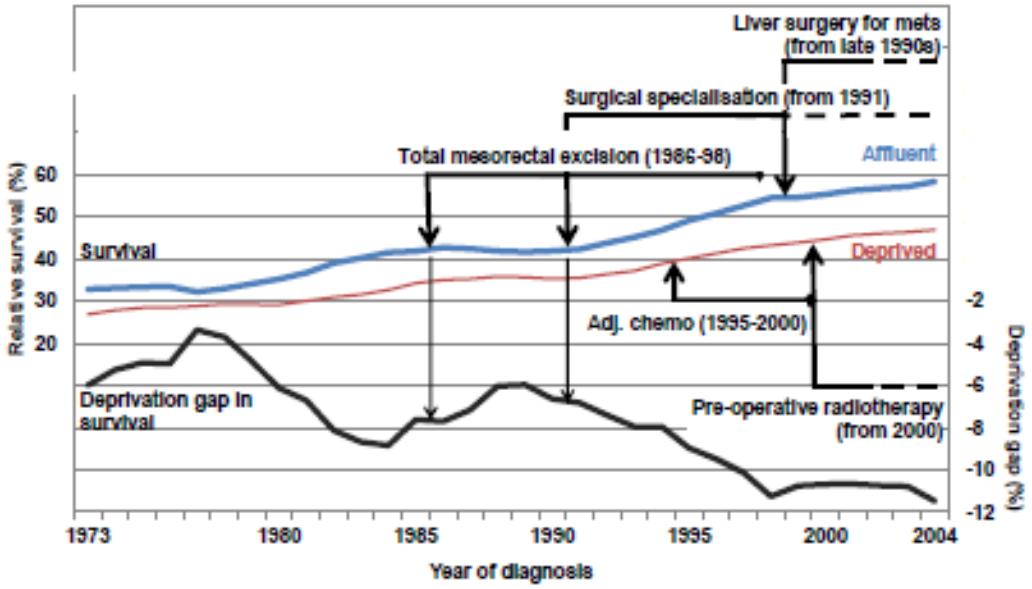


Figure 3. Trends in 5-year relative survival (%) from rectal cancer in men in the most affluent and most deprived groups, and the deprivation gap (%) in survival: 5-year moving average values, England and Wales, 1973-2004. Periods of emergence of evidence about the efficacy of new interventions are denoted on the graph. Increasing use of flexible sigmoidoscopy occurred throughout the study period, and is not denoted on the graph.



DISCUSSION

We report contrasting long-term trends in socio-economic inequalities in survival for two common cancers. For breast cancer in women, the deprivation gap in five-year survival narrowed slowly steadily from the early 1970s to the mid-2000s, whereas for rectal cancer in men, survival inequalities widened substantially over the 32-year period, but followed a more complex pattern with two periods of narrowing inequality. The findings extend the observation period of previously reported trends in overall survival,[9,10] and suggest that for breast cancer, the narrowing of the deprivation gap in survival continues a trend from the early 1970s.

Trends in socio-economic inequality in survival could relate to socio-economic differences in tumour factors (such as morphology and stage); patient factors (such as co-morbidity); healthcare factors (such as differential diffusion over time of effective new interventions), and non-cancer mortality.[1,2,32] For such factors to explain changes over time in survival inequalities, they should account for at least part of the deprivation gap at the start of the observation period, and also be considered capable of accounting for subsequent change in the deprivation gap over time.

Changes in the socioeconomic distribution of tumour morphology and biology (reflecting prior socioeconomic differences in exposure to risk factors associated with tumour types of different prognosis) are an unlikely explanation of the findings. Evidence for the role of tumour factor differences as determinants of socioeconomic inequalities in survival is inconsistent.[1] However, even if socioeconomic differences in risk factor exposure and tumour biology could explain survival inequalities cross-sectionally (i.e. at one point in time) for them to explain the continually narrowing survival gaps in breast cancer survival

during 1974-2006, they should have occurred continually during a period prior and during the examined study period. We know of no evidence detailing such 'convergence' or 'divergence' in socioeconomic differences in risk factor exposure or tumour type for either breast or rectal cancer. Moreover, in relation to rectal cancer, socioeconomic differences in exposure to risk factors associated with more aggressive (poorer prognosis) tumour types ought not only to have been substantial initially, but should have also changed 'direction' twice during a period prior and during the study. Therefore, although we acknowledge that socioeconomic differences in tumour biology could account for a proportion of the observed differences in survival inequalities, we believe they are unlikely to represent a substantial cause of the observed substantial changes over time in survival inequalities in major part.

Differential changes in the co-morbidity burden of cancer patients of different socioeconomic groups are also an unlikely explanation. Co-morbidity affects clinical decisions about treatment suitability; some research also postulates that it could lower host resistance to cancer.[33] No data were available on co-morbidity in the cancer patients we studied, but there is evidence of either stable or widening inequalities in general fitness and co-morbidity in both sexes during the study period.[34,35,36] Although widening inequalities in co-morbidity could perhaps have contributed to widening inequalities in rectal cancer survival, it would be hard for this to explain narrowing inequalities in breast cancer survival, as co-morbidities constraining treatment (such as obstructive lung disease and coronary artery disease) are the same for both cancers. Further, the direct effects of lethal co-morbidity are taken into account by the use of relative survival, which compensates for background mortality from other causes of death.

Changes over time in the socioeconomic distribution of mortality from unrelated causes, could in principle artificially 'inflate' or 'decrease' cancer survival.[32] However, this could not have biased the findings in relation to changes over time in survival inequality, because deprivation group-specific life tables were used.

Trends in the socioeconomic distribution of stage could in principle be relevant. Given the time period of our study (starting in 1973) no population-based data were available on tumour stage. Changes in mean stage at presentation are likely to have occurred during the study period, both because of secular improvements in patient and clinician awareness of early signs and symptoms of symptomatic disease, and because of organised screening activity. However, although differential improvement in stage at presentation in favour of more deprived patients could have been in part responsible for narrowing inequalities for breast cancer, it is difficult to reconcile this hypothesis with the observed increasing survival inequality observed for rectal cancer, which would have required inverse changes in the socioeconomic distribution of stage.

The introduction of breast cancer screening during the study period has contributed to distinct improvement in relative survival.[37] It is however unlikely that the introduction of breast screening could have contributed to narrowing survival inequalities, as screening uptake has been slightly higher among more affluent patients,[38,39] and therefore the net effect of such uptake differences could not have contributed the observed narrowing of survival inequalities.

Having considered the potential role of changes over time in socioeconomic differences in respect of tumour and patient factors, and in competing mortality, we would wish to draw attention to the potential role of socioeconomic differences in the speed of

dissemination of newer treatments among patients of different deprivation groups during the study period. Given the study period, we were not able to take into account in the analysis any information on the actual treatment provided to patients. For more recent periods, and prospectively, it is hoped that use of linked datasets (e.g. of cancer registration with Hospital Episodes Statistics data) could help more accurately depict treatment patterns in the future (including information on the timeliness, nature and 'dose' of treatments).[40] A key consideration is that following Victora's hypothesis survival inequalities can be considered to be the final product of successive inequality phases in relation to treatments introduced in temporal sequence. Therefore, whether inequalities get narrower or wider is determined by whether successive innovations in management are more or less effective compared with previous and subsequent treatment innovations.

Adjuvant chemotherapy, endocrine therapy (tamoxifen) and breast cancer screening were all introduced during the study period. Most (i.e. about two thirds) of the observed reduction in breast cancer mortality in England and Wales between 1971 and 1997 is attributable to wider availability and use of chemotherapy and endocrine therapy, as opposed to earlier diagnosis because of screening.[37] Concordant findings have been observed in the USA (1975-2000),[41] and Norway,[42] and also in Australia (1981-1994) where substantial improvement in survival had been achieved before screening programmes were introduced.[43] Therefore, the most effective (in terms of effect size) treatments for breast cancer during the study period appear to have been those relatively 'old' (but comparatively more effective) treatments gradually introduced in clinical practice during the 1970s and 1980s. Both adjuvant chemotherapy and endocrine therapy are associated with up to 30% reduction in mortality, an effect size substantially larger to that derived by screening (15%).[44] If a newer treatment is less

effective than an older one, survival inequality may narrow over time, because the lapse of a 'lag' period eventually enables equal use of the older and more effective treatment. The degree of 'inequality resolution' resulting from this change exceeds the 'inequality generation' resulting by the introduction of the newer (but less effective) treatment. Whilst a degree of inequality may prevail for relatively new interventions (such as breast cancer screening),[38,39] if their effect size is smaller than that of other, 'older' interventions, the net effect will be progressive narrowing of inequality – as observed in our study. Reduction of geographical inequalities in breast cancer survival between different regions against the background of improving overall population survival, were described in Denmark, reminiscent of our own findings,[45] which also concord with Australian research.[46] Evidence from The Netherlands confirms substantial changes in clinical management during the study period.[47]

Regarding rectal cancer, it has been postulated previously that widening survival inequalities for rectal cancer between 1986 and 1999 may have been caused by a combination of a differential socioeconomic trends in earlier diagnosis and clinical management.[48] Rectal cancer provides a good example of the multi-modality of cancer management, with several tests and treatments being of great relevance to clinical management – most of which have been introduced and disseminated into clinical practical gradually during the study period. Unlike breast cancer, it would appear that the succession of innovative treatments was 'from less to more efficacious', resulting in widening inequality. However, the relatively large number of innovations in rectal cancer management during the study period makes the detection of their direct impact on population survival (in the absence of direct empirical prospective evidence on treatment use) challenging.

We have used five-year relative survival. Trends in survival inequality can also be compared for any other time period, e.g. one-year, three-year and five-year conditional upon one-year survival. We have indeed calculated such survival estimates, but on inspection, it was apparent there was no added value in presenting such analyses. We opted to focus on inequalities in survival (as opposed in hazard of death) as survival is the most commonly used metric of population-based outcomes in cancer care, and so that our findings can be understood and interpreted more immediately by researchers, members of the public, and policy makers.[49] Although in principle the choice of absolute or relative measures of inequality could give different interpretations,[50,51] in our own study examining relative differences in survival identifies similar change patterns over time. There is no universal acceptance of consistently using either absolute or relative inequality measures, reason for which presenting actual (socioeconomic group specific) rates, as opposed to only presenting summary inequality measures such as rate differences or ratios is recommended,[50,51] and this is why we present actual rates as well as summary measures in our study.

We have examined and report opposing (narrowing-widening) inequality trends during a 32-year period for two common cancers and explored the potential role of different explanatory factors, and healthcare factors in particular. Although the analysis relates to historical data, our findings could hold valuable lessons for policy makers of the present day. Ongoing investment in prospective national audit datasets and registries could help to track diffusion of effective innovation in cancer treatment more effectively than it has been possible in the past, and help detect potential variation in use among different population subgroups. Such policy initiatives that could enable the 'early detection' of inequality in process measures such as treatment use, help 'reduce' the length of 'natural' treatment inequality lags resulting from the introduction of new treatments, and

accelerate the reduction of historical or prevent the generation of future inequalities in outcomes. Further studies including prospective data collection of treatment details could help amplify the empirical basis supporting the interpretation framework about social inequalities in survival that we propose in this paper.

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Figure legends

Figure 1.

Figure 1. When an effective new treatment (A) first becomes available, its use is initially higher among more affluent patients. Later, uptake increases among more deprived patients, eventually catching up with levels in affluent groups. Equal use of the treatment is reached after a lag period has elapsed. However the cycle may start again, for another, newer, treatment (B), giving rise to another inequality-equality lag cycle, and perpetuating socio-economic inequalities in healthcare.

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Figure 3. Trends in 5-year relative survival (%) from rectal cancer in men in the most affluent and most deprived groups, and the deprivation gap (%) in survival: 5-year moving average values, England and Wales, 1973-2004. Periods of emergence of evidence about the efficacy of new interventions are denoted on the graph. Increasing use of flexible sigmoidoscopy occurred throughout the study period, and is not denoted on the graph.

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