RESEARCH ARTICLE

Influence of Payer Source on Treatment and Outcomes in Colorectal Cancer Patients in a University Hospital in Thailand

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Abstract

The study aimed to compare the 2 main types of insurance used by colorectal cancer (CRC) patients in a university hospital in Thailand: universal coverage (UC) and 'Civil Servant Medical Benefit Scheme' (CSMBS) in terms of hospital expenditure and survival outcomes. CRC cases in stages I-IV who were operated on and had completed their adjuvant therapy in Songklanagarind Hospital from 2004 through 2013 were retrospectively reviewed regarding their hospital expenditure, focusing on surgical and chemotherapy costs. Of 1,013 cases analyzed, 524 (51.7%) were in the UC group while 489 (48.3%) belonged to the CSMBS group. Cases with stage IV disease were significantly more frequent in the UC group. Average total treatment expenditure (TTE) was 143,780 Thai Baht (THB) (1 US$ =~ 30 THB). The TTE increased with tumor stage and the chemotherapy cost contributed the most to the TTE increment. TTE in the CSMBS group was significantly higher than in the UC group for stage II-III CRCs. The majority of cases in the UC group (65.5%) used deGramont or Mayo as their first line regimen, and the proportion of cases who started with a capecitabine-based regimen (XELOX or Xeloda®) was significantly higher in the CSMBS group (61.0% compared to 24.5% in the UC group, p-value < 0.01). On survival analysis, overall survival (OS) and progress free survival in the CSMBS group were significantly better than in the UC group. The 5-year OS in the CSMBS and UC groups were 84.3% and 74.6%, respectively (p-value < 0.01). In conclusion, the study indicates that in Thailand, the type of insurance influences resource utilization, especially the choice of chemotherapy, in CRC cases. This disparity in treatment, in turn, results in a gap in treatment outcomes.

Keywords: Colorectal cancer - universal coverage - health care scheme - treatment outcome

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Introduction

Colorectal cancer (CRC) has been increasing in significance in middle-income countries like Thailand, where the incidence has been inflating with urbanization (Khuhaprema and Srivatanakul, 2008; Center et al., 2009a; Myong et al., 2012). CRC is a good model of a human cancer that has benefited from modern cancer therapy, including modern adjuvant therapy and laparoscopic surgery. In the United States, the healthcare cost of CRC is increasing while the mortality rate has been declining in recent years (Center et al., 2009b; Seal et al., 2013). However, not all groups have benefited equally from advanced treatment as recent studies showed that patients with private insurance had better overall and stage-specific survival when compared with patients who were uninsured or insured by Medicaid or Medicare (Ward et al., 2008; Robbins et al., 2009). The evidence suggests that policy variations caused by different payer sources might influence the treatment pattern and outcome of various diseases, including CRC.

In Thailand, there are 4 main types of health insurance: 1) 'Universal Coverage' (UC) a public medical benefit provided free-of-charge by the Thai government for all Thai citizens, 2) 'Civil Servant Medical Benefit Scheme' (CSMBS) an employment benefit provided for government officials, 3) the 'Social Security Scheme' a co-pay insurance available for non-governmental employees and 4) private insurance (Towse et al., 2004; Garabedian et al., 2012). The first 2 types (UC and CSMBS) cover a majority of the payer sources in our institute, a university hospital in the southern part of the country. Differences exist regarding reimbursement of treatment provided between the 2 schemes. In the UC group, for example, reimbursement can be made only for drugs in the National Drug List while almost all drugs can be chosen according to their indication in the CSMBS group. In addition, reimbursement in the UC group is capitated by disease related group (DRG) system. This has then raised the question as to whether this disparity

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in the incentive provided by different insurance plan results in discrepancies in the treatment outcomes in our CRC patients.

This study aimed to compare the treatment expenditure, treatment pattern and outcomes between CRC patients who used UC and those who used CSMBS as their main payer source. We hypothesized that limited reimbursement policy in the UC group may affect the treatment outcome.

Materials and Methods

The study design was a retrospective hospital-based cohort of CRC cases stage I-IV who were operated on and had completed their adjuvant therapy in Songklanagarind Hospital during the years 2004-2013. The hospital is a model of government-run tertiary level hospital, in which the majority of patients hold one of insurance provided by the central government, either UC or CSMBS. The cases were identified through the records of the Cancer Registry Unit, Faculty of Medicine, Prince of Songkla University. General demographic data, surgical procedures, surgical complications, adjuvant treatment and follow-up data were retrieved from the electronic medical records database of the hospital. Treatment expenditure was defined as total in-hospital expenditure incurred during the period of definitive cancer treatment, which mainly included the surgery and adjuvant treatment plus outpatient chemotherapy costs. Chemotherapy expenditure included both inpatient and outpatient chemotherapy sessions. Surgical expenditure included the operative costs and perioperative care during the same admission. All prices were calculated as 2013 equivalent prices by using Consumer Price Index (CPI) values provided by the Bank of Thailand. Access to clinical records and financial data was approved by the institutional Research Ethics Committee.

Primary tumor staging for all of the study patients followed the sixth edition of the TNM staging system of the American Joint Committee on Cancer (AJCC). Adjuvant chemotherapy was considered for stage III colonic cancer patients, and adjuvant chemo-radiation was considered for stages II and III rectal cancer cases. Patients who received neoadjuvant treatment were not included in this study. Lymph node number was used as a quality indicator in this study and the cutoff level at 12 nodes was used according to the recommendation of the American Society for Clinical Oncology and the US National Quality Forum (Wong et al., 2007) and our previous study (Kritsanasakul et al., 2012).

All patients were evaluated for at least 1 year after surgery or until death. Follow-up visits were scheduled according to the chemotherapy intervals during the first year after surgery, every 3 months during the second year, every 6 months until the fifth year and annually thereafter.

Survival times were calculated from hospital-based data from the electronic hospital information system and/or death registry data from the database of the institutional Cancer Registry Unit, as of February 2014. Continuous demographic data are presented as mean and range if not stated otherwise. Cancer death was regarded as failure in the Kaplan-Meier survival analysis for the overall survival (OS). Local relapse, new metastasis, second malignancy and death were regarded as progress in progress-free survival (PFS) analysis. Univariate survival analysis used the Log-rank test and Cox proportional hazard analysis. A p-value of less than 0.05 was considered statistically significant. All analysis was done using the Stata version 6.0 program (Stata Corporation, College Station, TX).

Results

Demographic data and CRC management

One thousand one hundred and twenty one cases of CRC (603 males and 518 females) who were operated on in Songklanagarind Hospital during the years 2004 and 2013 and had completed their treatment according to the standard guideline of the Institute were analyzed. The average age of the patients was 64.6 years (range 23-99 years). Of 1,121 patients, 524 cases (46.7%) used the UC as their payer source, 489 cases (43.6%) used the CSMBS, 40 cases (3.6%) used the social security insurance, 3 cases (0.2%) used private insurance and 65 cases (5.8%) paid the treatment fee themselves with no insurance claim. As the study focused on only the 2 main payer-sources, the study analyses were limited to the 1,013 cases that belonged to the UC and CSMBS groups.

The 1,013 cases included 487 cases of colon cancer (48.1%) and 526 cases of rectal cancer (51.9%). Stage distributions were localized tumor (AJCC stage I and II) in 400 cases (39.6%), loco-regional disease (stage III) in 425 cases (42.0%), distant metastasis (stage IV) in 186 cases (18.4%), and the remaining 2 cases did not have completed staging data. Patients with distant metastasis were significantly higher in the UC group than the CSMBS group (24.3% *vs* 12.1%) (p-value <0.01). Other demographic parameters did not have statistically significant differences between the 2 groups (Table 1). Regarding comorbidity, the proportion of patients with a high number of comorbidities (more than 2 items) was significantly higher in the CSMBS group (Table 1). Three comorbidities that had significantly higher frequency in the CSMBS group were hypertension, dyslipidemia and ischemic heart disease.

Comparisons of actual treatment details are displayed in Table 1. CRC patients receiving chemotherapy were significantly higher in the UC group when all stages were analyzed together. However, when only stages II and III were considered, the chemotherapy rate at 69% in the UC group and 65% in the CSMBS group were not statistically different. Radiation therapy was given to rectal cancer patients at rates of around 49% in the UC group and 40% in the CSMBS group. Use of molecular targeted therapy was not common in our patients at the study period (7.7 % of overall cases and 11.8% of stage IV cases). There was a slightly higher percentage of targeted therapy used in the CSMBS group; however, the difference was not statistically significant.

Considering adjuvant treatment, 644 of 1,013 patients (63.6%), including 26 cases (24.1%) in stage I, 167 cases in stage II (57.2%), 325 cases (76.5%) in stage III and 124 cases (66.7%) in stage IV, received adjuvant chemotherapy. Of the cases who received chemotherapy,

462 cases (74.2%) received 5-Fluorouracil (5-FU)/ Leucovorin (LV) or Capecitabine monotherapy as their first regimen. The majority of UC patients received 5-FU/ LV as their first regimen (65% compared to 23.5% in CSMBS, p-value < 0.01) when almost 40% of CSMBS cases started with Capecitabine monotherapy (XELODA).

Table 1. Comparisons of Demographic Data, Comorbidity and Actual Treatment between the 2 Groups of Colorectal Cancer Patients. UC: Universal Coverage, CSMBS: Civil Servant Medical Benefit Scheme

Parameter	UC	CSMBS	p-value**
All (1,013 cases)	524 (51.7%)	489 (48.3%)	
General data			
Tumor site			0.26
Colon	243 (46.4%)	244 (49.9%)	
Rectum	281 (53.6%)	245 (50.1%)	
AJCC stage*			< 0.01
Stage I	39 (7.5%)	69 (14.1%)	
Stage II	131 (25.1%)	161 (32.9%)	
Stage III	225 (43.1%)	200 (40.9%)	
Stage IV	127 (24.3%)	59 (12.1%)	
CEA*			0.08
0-5 mg/dl	261 (51.8%)	266 (57.3%)	
> 5 mg/dl	263 (48.2%)	198 (42.7%)	
Tumor differentiation*			0.41
Well	260 (50.6%)	266 (54.6%)	
Moderate	225 (43.8%)	193 (39.6%)	
Poor	29 (5.6%)	28 (5.8%)	
Mode of surgery*			0.74
Elective	482 (92.5%)	455 (93.1%)	
Emergency	39 (7.5%)	34 (7.0%)	
Lymph node ratio			0.07
0-0.35	401 (82.2%)	402 (86.5%)	
> 0.35	87 (17.8%)	63 (13.6%)	
Year of surgery			0.71
AC 2004-2008	243 (46.3.2%)	221 (45.2%)	
AC 2009-2013	281 (53.6.8%)	268 (54.8%)	
Comorbidity***			
Ischemic heart disease	12 (2.3%)	22 (4.6%)	0.049
Diabetes mellitus	52 (10.2%)	51 (10.7%)	0.77
Hypertension	92 (18.0%)	117 (24.6%)	0.01
Chronic lung disease	6 (1.2%)	10 (2.1%)	0.25
Dyslipidemia	23 (4.5%)	38 (7.9%)	0.03
Number of comorbidity			< 0.01
0 item	354 (69.3%)	299 (63.0%)	
1-2 items	147 (28.8%)	149 (31.4%)	
3-4 items	10 (2.0%)	27 (5.7%)	
Surgery			
Open colectomy	428 (81.7%)	367 (75.1%)	< 0.01
Laparoscopic colectomy	59 (11.3%)	96 (19.6%)	
Hartmann procedure and others	37 (7.1%)	26 (5.3%)	
Quality of operation			< 0.01
Node number < 12 nodes	168 (33.7%)	201 (42.6%)	
Node number > 12 nodes	331 (66.3%)	271 (57.4%)	
Adjuvant			
Chemotherapy (all stages)			< 0.01
No	162 (30.9%)	207 (42.3%)	
Yes	362 (69.1%)	282 (57.7%)	
Chemotherapy (stage II-III)			0.06
No	100 (28.1%)	125 (34.6%)	
Yes	256 (71.9%)	236 (65.4%)	
Targeted therapy			0.13
No	490 (93.5%)	445 (91.0%)	
Yes	34 (6.5%)	44 (9.0%)	
Radiation therapy (rectal cancers)			0.05
No	144(51.3%)	145(59.7%)	
Yes	137(48.8%)	98(40.3%)	

*Missing data exists, ** all comparisons were mabe by Chi-square test *** Co-morbidities were hospital-based data, CEA: Carcinoembryonic Antigen

Significantly more cases in the CSMBS group (94 cases, 34.6% of chemotherapy receivers) received combination therapy (FOLFOX, FOLFIRI or XELOX) than in the UC group (53 cases, 15.1%) (p-value < 0.01).

Treatment expenditure and payer-source distribution

Average total treatment expenditure (TTE) was 143,780 THB (4,793 US$), ranging 4,362 THB-1,739,553 THB. The average surgical expenditure (35,901 THB) and the average chemotherapy expenditure (84,722 THB) contributed 25.0 % and 58.9 % of the TTE in our patients, respectively. The TTE increased, with tumor stage and chemotherapy expenditure contributed the most to the increment (Figure 1).

The overall TTE in the CSMBS group (164,493 THB) was higher than that of the UC group (124,736 THB) (p-value < 0.01). Considering each stage separately, the difference was at statistically significant level in stage II and III CRC only (Figure 2 and Table 2).

Treatment outcome comparison

Length of hospital stay during the surgical admission in the UC group (15.0 days) was significantly longer than in the CSMBS group (13.5 days). The reported incidence of surgical complications was significantly more in the UC group, while chemotherapy complications occurred in higher frequency in the CSMBS group. The mean follow-up duration was 59 months (range 6 months-122 months). On survival analysis, the 5-year OS was 79.2%; 92.6% in stage I, 88.3% in stage II, 76.3% in stage III and 60.9% in stage IV CRC. The 5-year PFS was 70.0%, 93.4% in

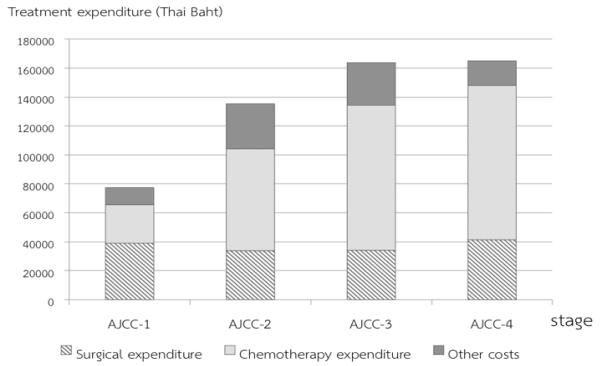

Figure 1. Total Treatment Expenditure According to Tumor Stage and its Composition

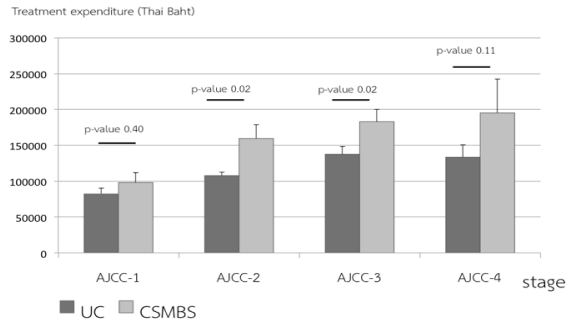

Figure 2. Comparing Total Treatment Expenditure between 2 Payer Sources According to Stage. UC: Universal Coverage, CSMBS: Civil Servant Medical Benefit Scheme

Table 2. Treatment Expenditure and Outcome Comparisons between 2 Payer-Source Groups UC: Universal Coverage CSMBS: Civil Servant Medical Benefit Scheme, OS: Overall Survival, PFS: Progress-free Survival

Category	UC	CSMBS	p-value*
Treatment expenditure			
Total expenditure			
Stage I	82,214	98,289	0.4
Stage II	159,647	107,819	0.02
Stage III	183,037	137,630	0.02
Stage IV	195,364	133,556	0.11
Surgery			
Stage I	36,348	40,557	0.47
Stage II	44,636	25,104	<0.01
Stage III	40,519	27,108	<0.01
Stage IV	46,336	30,791	0.08
Chemotherapy			
Stage I	20,175	30,116	0.61
Stage II	24,403	107,944	<0.01
Stage III	59,209	146,165	<0.01
Stage IV	78,282	169,752	0.03
Outcomes			
Length of hospital stay	15.0 days	13.5 days	< 0.01*
Operative complication	13.90%	9.60%	0.03**
Chemotherapy complication	15.30%	27.20%	< 0.01**
5-year OS			
All stages	74.60%	84.30%	< 0.01***
AJCC II-III	78.80%	84.20%	0.02
5-year PFS			
All stages	60.60%	79.80%	< 0.01
AJCC II-III	68.00%	80.50%	< 0.01

*unpaired T-test, **Chi-square test, *** Log-rank test

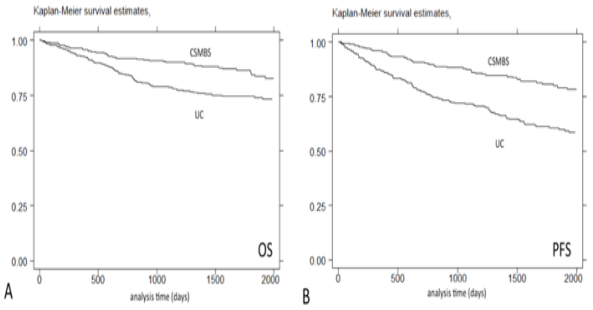

Figure 3. Kaplan-Meier Survival Curves Showing Overall Survival (OS) and Progress-free Survival (PFS) Comparisons between the Civil Servant Medical Benefit Scheme (CSMBS) and Universal Coverage (UC) (p-values Calculated by Log-Rank Test)

stage I, 82.9% in stage II, 67.2% in stage III and 38.2% in stage IV CRC.

Survival (both OS and PFS) in the CSMBS group was significantly better than in the UC group (Log-rank p-value < 0.01). In order to reduce the effect of unequal distribution of stages between the 2 payer-source groups, the survival analyses were repeated in stages AJCC II-III. Both OS and PFS in the SCMBS group remained significantly higher than that of the UC group.

On unadjusted Cox's hazard analysis, the UC group had a higher probability of CRC related death than the CSMBS group, with a hazard ratio of 1.8 (95% confidence interval 1.3-2.5).

Discussion

It has recently been estimated that treatment of CRCs comprises approximately 12% of all cancer costs (Gellad and Provenzale, 2010). Factors that directly affect treatment costs include cancer site, stage at diagnosis, age at diagnosis, and phase of treatment (Lang et al., 2009). In addition, indirect factors that may influence decision-making in resource utilization of the health care provider include socioeconomic status and insurance status. Disparities in the treatment may result in outcome disparities between those able to afford better treatment options and those who cannot. A study in breast cancer patients demonstrated that patients with different socioeconomic status are likely to receive different types of diagnostic procedures and surgeries (Azzopardi et al., 2014; Chang et al., 2014). In CRCs, a 2001 review from the United States showed poorer survival outcomes in CRC patients with lower socioeconomic status (Hodgson et al., 2001). Such disparities can be a result of either more delayed diagnosis or inferiority in standard of care in the poorer patients.

The UC scheme in Thailand was launched as part of a nationwide Health system reform in 2001 under the scheme of '30-Baht treats all' program- any citizen without other insurance could go to the hospital for any problem and pay approximately 1 US dollar for any treatment. The scheme was designed to provide a basic health protection plan for all Thai people. In this program, in-patient care is reimbursed from a provincial budget based on a weight of the diagnosis related group (DRG) (Towse et al., 2004). Under this policy, drug utilization is limited to the National Essential Drug List (Garabedian et al., 2012), which means that, in CRCs, only conventional regimen that contain 5-fluorouracil and leucovorin (deGramont and Mayo) can be prescribed unless the patient changes the payment type. In the patients registered as UC type, costs incurred by a regimen containing oxalipatin, irinotecan or oral capecitabine-based chemotherapy needs to be absorbed out-of-pocket, but for patients with CSMBS, these costs are all reimbursed by the Government. Utilization of modern drugs is thus largely restricted to the latter group. In 2012, a study from a university hospital in the north-eastern part of the country also reported that hospital treatment costs in CRC were highest in CSMBS patients and lowest among UC holders (Chindaprasit et al., 2012). We also analyzed co-morbidities between the two groups and found paradoxically higher incidence of co-morbidity in the CSMBS group. The data strongly suggesting that difference in treatment was probably the main factor in the outcome gap between the two groups. Although our study did not attempt to compare the treatment efficacy of any specific treatment, it could be speculated that the difference in adjuvant chemotherapy regimens available for the differently insured groups was one of the factors that explains the outcome disparity. These findings are also consistent with a nation-wide study comparing survival outcome in patients with lymphoma between those with UC and those with CSMBS. The study demonstrated inferior PFS in the UC group, and suggested

the inaccessibility of targeted therapy (rituximab) could explain the disparity (Intragumtornchai et al., 2012).

Another dissimilarity that may explain the outcome gap was the higher disease severity in the UC group as defined by higher frequency of stage IV and higher CEA. However, when only stage II and III subgroups were analyzed, the PFS in the UC group remained inferior.

A standard practice guideline and quality monitoring might be effective measures to reduce the outcome gap in cases where different insurance plans necessitate differing treatment plans (Riley et al., 2008). As new treatment modalities are launched into the market and inflation leads to treatment cost increases, disparities in terms of accessibility and treatment outcome will also become more severe. It was estimated that the treatment cost of CRCs increased by 73% from 2005 to 2009 (Seal et al., 2013). In Thailand, as the insurer of both major health care schemes, the government needs to monitor new technologies and establish guidelines for rational use of novel chemotherapeutic agents. While the drug list for the UC needs to be expanded, resource utilization in the CSMBS also may need to be monitored. In addition, factors identifying high-risk patients who require more intensive therapy need to be identified and put into the treatment algorithm. Based on our scenario, each percent increase in the 5-year OS in one CRC patient will cost 4,097 THB.

Limitation of our study was at the retrospective review of hospital-record. Significant unrecorded data such as co-morbidities, treatment outside the hospital and discrepancy in referral pattern between groups may exist.

In conclusion, the study compared hospital expenditures in the whole treatment course of CRCs between the two main types of insurance used in a university hospital. The study found significantly higher costs in the CSMBS 'superior insurance' group, which may explain the better survival outcome.

References

Azzopardi J, Walsh D, Chong C, et al (2014). Surgical treatment for women with breast cancer in relation to socioeconomic and insurance status. *Breast J*, **20**, 3-8.

Center MM, Jemal A, Smith RA, et al (2009). Worldwide variations in colorectal cancer. *CA Cancer J Clin*, **59**, 366-78.

Center MM, Jemal A, Ward E (2009). International trends in colorectal cancer incidence rates. *Cancer Epidemiol Biomarkers Prev*, **18**, 1688-94.

Chang TS, Huang KY, Chang CM, et al (2014). The association of hospital spending intensity and cancer outcomes: a population-based study in an Asian country. *Oncologist*, **19**, 990-8.

Chindaprasit J, Sookprasert A, Wirasorn K, et al (2012). Cost of colorectal cancer care in hospitalized patients of Thailand. *J Med Assoc Thai*, **95**, 196-200.

Myong JP, Kim HR (2012) Impacts of household income and economic recession on participation in colorectal cancer screening in Korea. *Asian Pac J Cancer Prev*, **13**, 1857-62.

Garabedian LF, Ross-Degnan D, Ratanawijitrasin S, et al (2012). Impact of universal health insurance coverage in Thailand on sales and market share of medicines for non-communicable diseases: an interrupted time series study. *BMJ Open*, **2**, e001686.

Gellad ZF, Provenzale D (2010). Colorectal cancer: national and international perspective on the burden of disease and public health impact. *Gastroenterology*, **138**, 2177-90.

Hodgson DC, Fuchs CS, Ayanian JZ (2001). Impact of patient and provider characteristics on the treatment and outcomes of colorectal cancer. *J Natl Cancer Inst*, **93**, 501-15.

Intragumtornchai T, Bunworasate U, Siritanaratkul N, et al (2013). Inferior progression-free survival for Thai patients with diffuse large B-cell lymphoma treated under Universal Coverage Scheme: the impact of rituximab inaccessability. *Leuk Lymphoma*, **54**, 83-9.

Khuhaprema T, Srivatanakul P (2008). Colon and rectum cancer in Thailand: An Overview. *Jpn J Clin Oncol*, **38**, 237-43.

Kritsanasakul A, Boonpipattanapong T, Wanitsuwan W, et al (2012). Impact of lymph node retrieval on surgical outcomes in colorectal cancers. *J Surg Oncol*, **106**, 238-42.

Lang K, Lines LM, Lee DW, et al (2009). Trends in healthcare utilization among older Americans with colorectal cancer: a retrospective database analysis. *BMC Health Serv Res*, **9**, 227.

Riley GF, Warren JL, Potosky AL (2008). Comparison of cancer diagnosis and treatment in Medicare fee-for-service and managed care plans. *Med Care*. **46**, 1108-15.

Robbins AS, Pavluck AL, Fedewa SA, et al (2009). Insurance status, comorbidity level, and survival among colorectal cancer patients age 18 to 64 years in the National Cancer Data Base from 2003 to 2005. *J Clin Oncol*, **27**, 3627-33.

Seal BS, Sullivan SD, Ramsey S, et al (2013). Medical costs associated with use of systemic therapy in adults with colorectal cancer. *J Manag Care Pharm*, **19**, 461-7.

Towse A, Mills A, Tangcharoensathien V (2004). Learning from Thailand's health reforms. *BMJ*, **328**, 103-5.

Ward E, Halpern M, Schrag N, et al (2008). Association of insurance with cancer care utilization and outcomes. *CA Cancer J Clin*, **58**, 9-31.

Wong SL, Ji H, Hollenbeck BK, et al (2007). Hospital lymph node examination rates and survival after resection for colon cancer. *JAMA*, **298**, 2149-54.