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Time trends in chemotherapy (administration and costs) and relative survival in stage III colon cancer patients – a large population-based study from 1990 to 2008

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Abstract

Background. Use of adjuvant chemotherapy for stage III colon cancer has increased since several trials have shown the beneficial effect on survival. In this population-based study we show time trends in the administration and costs of chemotherapy and relative survival of patients with stage III colon cancer. *Methods.* All patients surgically treated for adenocarcinoma of the colon stage III between 1990 and 2008 in The Netherlands were included. Relative survival (using period analyses) and Relative Excess Risks of death (RER) were calculated. The costs of chemotherapy were estimated. *Results.* A total of 24 111 colon cancer patients with stage III were included in the cohort. The administration (from 9.5% in 1990 to 61.8% in 2008; $p < 0.001$) and costs of chemotherapy (from €38 467 in 1990 to €3 876 150 in 2008) increased during the study period. Multivariable relative survival improved for patients receiving adjuvant chemotherapy (RER 0.93; 95% CI 0.92–0.94; $p < 0.001$). In contrast, relative survival remained stable for patients, younger than 80 years, who did not receive chemotherapy (RER 1.00; 95% CI 1.00–1.01; $p = 0.3$). Patients aged 80 years and older without chemotherapy, relative survival increased during the study period (RER 0.98; 95% CI 0.97–0.99; $p < 0.001$). *Conclusions.* The administration, the costs of chemotherapy and the survival of patients with stage III colon cancer increased over time. Whereas the costs and administration of chemotherapy increased extensively, relative survival increased to a lesser extent. For patients treated with adjuvant chemotherapy relative survival increased equally in all age groups.

Colorectal cancer is one of the most frequently diagnosed cancers in The Netherlands with more than 12 000 new patients annually. Approximately, two thirds of the patients are diagnosed with colon cancer and approximately one quarter of these patients are diagnosed with stage III disease [1]. After potentially curative surgery without adjuvant treatment, 50–60% of these patients will relapse [2]. Over 50% of the patients diagnosed with colon cancer are aged 70 years or older.

Moertel et al. were first to show a significant decrease in recurrence and improvement in survival of stage III colon cancer patients with the use of adjuvant fluorouracil and levamisole [3]. Afterwards, several studies have shown that levamisole can be replaced by folinic acid, whereas low dose folinic acid is as effective as high dose. Besides, it was shown that adjuvant chemotherapy for half a year achieves similar results in terms of relapse and improvement of survival as chemotherapy for one year [4,5]. In 2004 the MOSAIC-trial was published, which randomised between fluorouracil and folinic acid with or without oxaliplatin. The addition of oxaliplatin showed a significant increase in disease free

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survival and overall survival for stage III colon cancer patients [6]. A meta-analysis of recent trials showed no difference between oral or intravenous fluorouracil, and one trial included in the meta-analysis showed a trend towards an advantage in disease free survival for oral fluorouracil (capecitabine) [7].

In The Netherlands adjuvant chemotherapy for stage III colon cancer patients was incorporated in the guidelines in the mid-1990s without age limits [8]. The guidelines advised half a year of fluorouracil in combination with folinic acid as adjuvant treatment. Revisions of the guidelines were made in 2004, when FOLFOX (a combination of fluorouracil, folinic acid and oxaliplatin) was advised. Since 2008 the guidelines included that intravenous fluorouracil could be replaced with oral fluorouracil (capecitabine). Furthermore, in case of high age and/or comorbidities, the medical oncologist can choose for monotherapy with oral fluorouracil [8].

In the aforementioned adjuvant trials, treatment was shown to be cost-effective, but elderly patients were usually not included. A large proportion of the elderly patients with stage III colon cancer do not receive adjuvant chemotherapy, although some studies showed a benefit for the elderly in terms of recurrence and survival [9,10]. In this population-based study we show time trends for young and elderly patients in the administration and costs of chemotherapy, and the survival of stage III colon cancer patients.

Patients and methods

Patients and follow-up

Patients were selected from The Netherlands Cancer Registry (NCR). The NCR is based on notification of all newly diagnosed malignancies in The Netherlands by the registry of histo- and cytopathology (PALGA-system). The National Hospital Discharge Databank, which receives discharge diagnoses of admitted patients from all Dutch hospitals, completed case ascertainment. Information on patient characteristics, such as gender and date of birth, as well as tumour characteristics, such as date of diagnosis, anatomical location [International Classification of Diseases for Oncology (ICD-O)], histology, stage (clinical and pathological TNM classification), grade, and primary treatment, were obtained routinely from the medical records, around nine months after diagnosis. The information about the primary treatment included whether patients received chemotherapy, but no information about the number of cycles or which drugs were retrieved. Completeness of data was estimated to be at least 95% [11]. The vital status was obtained either directly from medical records or through linkage of the cancer registry data with the municipal population registry which registers information on inhabitants' vital status.

Stage was based on pathological TNM classification (5th edition); if pathological stage was unknown, clinical TNM-stage was used. In approximately 1.2% of the patients the pN-stage were missing, resulting in the use of cN-stage. From 2003 the percentage of missing pN-stage decreased to approximately 0.2% per year. Patients were divided into four age groups (<60, 60–69, 70–79, and ≥ 80 years). Tumour localisation was categorised into the following anatomical locations: proximal colon; consisting of caecum, appendix, ascending colon, hepatic flexure, and transverse colon (ICD-O C18.0–C18.4), distal colon; consisting of splenic flexure, descending colon, and sigmoid colon (ICD-O C18.4–C18.7), and Not Otherwise Specified (NOS); consisting of unknown location or overlapping anatomical locations of the colon (ICD-O C18.8 and C18.9). The type of hospital was divided into two groups. Most patients were treated in non-university hospitals.

Patients with their first primary invasive colon cancer (adenocarcinoma; ICD-O C18) stage III (T1–4, N1–3, M0) diagnosed between January 1, 1990 and December 31, 2008 and surgically treated were selected from the NCR ($n = 24\ 111$). At least 98.8% of the included patients were treated with curative surgery.

Statistical analyses

Differences between the age groups were tested with a χ^2-test. Statistical significance was defined as $p < 0.05$.

Follow-up time was calculated as the time from diagnosis to death, last date of follow-up or last date of linkage with the municipal population registry (January 1, 2010). For survival analyses, overall survival and relative survival were calculated. Overall survival analyses were carried out by the Kaplan-Meier method and multivariable Cox proportional hazard models with any death as event. Relative survival was calculated by the Hakulinen method, as the ratio of the observed survival among the cancer patients and the survival that would have been expected based on the corresponding (age, sex, and year) general population. National life tables were used to estimate the expected survival. Relative Excess Risks of death (RER) were estimated using a multivariable generalised linear model with a Poisson distribution, based on collapsed relative survival data, using exact survival times. Period analysis was conducted for patients diagnosed between 2005 and 2008 [12]. The multivariable relative survival analysis was stratified for age groups

and adjuvant chemotherapy, as the model showed statistical interaction between the year of diagnosis, adjuvant chemotherapy, and age.

Costs of chemotherapy per vial or tablet were retrieved from the pharmacy at the Leiden University Medical Center for three years: 1990, 1999, and 2008. The costs presented in this study are solely the costs of the chemotherapy and were calculated per average person (height of 1.70 m, weight of 76 kg, and 1.90 m^2 body surface). The number of patients receiving chemotherapy was retrieved from the present dataset. The different types of chemotherapy and completion rate were unknown in the dataset retrieved from the NCR and were therefore retrieved from the 'Quality Information System Colorectal Cancer' project from the Comprehensive Cancer Centre The Netherlands, location Leiden, and extrapolated to the dataset from the NCR. The 'Quality Information System Colorectal Cancer' project was a project from 2004 until 2006 collecting detailed information about chemotherapy (type, dose and completion) of colorectal cancer patients in this region. Percentages from this project have been used to calculate the results in the current study, assuming that this region is representative for all the Netherlands. Patients who did not complete their chemotherapy were calculated to have had half of the courses of chemotherapy.

Results

A total of 24 111 colon cancer patients with stage III were included in the cohort. Median age of the patients at diagnosis was 70 (range 11–100) years. The age distribution was stable over time from 1990 to 2008 ($p = 0.7$). The sex distribution was different within the age groups, with more females in the elderly age group ($p < 0.001$, Table I). The distribution of anatomical tumour location changed with age, younger patients were more often diagnosed with distal tumours, while elderly patients were more often diagnosed with proximal tumours ($p < 0.001$). With increasing age, patients were more often diagnosed with higher T-stage ($p < 0.001$) and lower N-stage ($p < 0.001$).

Administration of chemotherapy

The administration of chemotherapy increased from 22.2% in 1990 to 92.3% in 2008 for patients younger

Table I. Patient characteristics.

	< 60 years	%	60–70 years	%	70–80 years	%	≥ 80 years	%	p-value
Sex									< 0.001
Male	2621	50.9	3420	53.7	3730	47.1	1564	33.5	
Female	2524	49.1	2943	46.3	4198	52.9	3111	66.5	
Period									0.7
1990–1996	1532	29.8	1881	29.6	2341	29.5	1415	30.3	
1997–2002	1647	32.0	2000	31.4	2579	32.5	1455	31.1	
2003–2008	1966	38.2	2482	39.0	3008	38.0	1805	38.6	
Grade									< 0.001
I	339	6.6	450	7.1	473	6.0	270	5.7	
II	3193	62.1	4078	64.1	4950	62.4	2752	58.9	
III	1197	23.3	1394	21.9	1912	24.1	1303	27.9	
Unknown	416	8.1	441	6.9	593	7.5	350	7.5	
Anatomical location									< 0.001
Proximal	2301	44.7	3081	48.4	4399	55.5	2895	61.9	
Distal	2742	53.3	3170	49.8	3397	42.8	1697	36.3	
NOS*	102	2.0	112	1.8	132	1.7	83	1.8	
T-stage									< 0.001
1	66	1.3	73	1.2	61	0.8	41	0.9	
2	385	7.5	487	7.6	589	7.4	274	5.9	
3	3875	75.3	4787	75.2	5904	74.5	3416	73.1	
4	805	16.6	997	15.7	1351	17.0	932	19.9	
Unknown	14	0.3	19	0.3	23	0.3	12	0.2	
N-stage									< 0.001
1	3589	69.8	4520	71.0	5796	73.1	3453	73.9	
2	1435	27.9	1706	26.8	1986	25.1	1123	24.0	
3	121	2.3	137	2.2	146	1.8	99	2.1	
Chemotherapy									< 0.001
Yes	3775	73.4	4066	63.9	2822	35.6	142	3.0	
No	1370	26.6	2297	36.1	5106	64.4	4533	97.0	
Total	5145	21.3	6363	26.4	7928	32.88	4675	19.4	

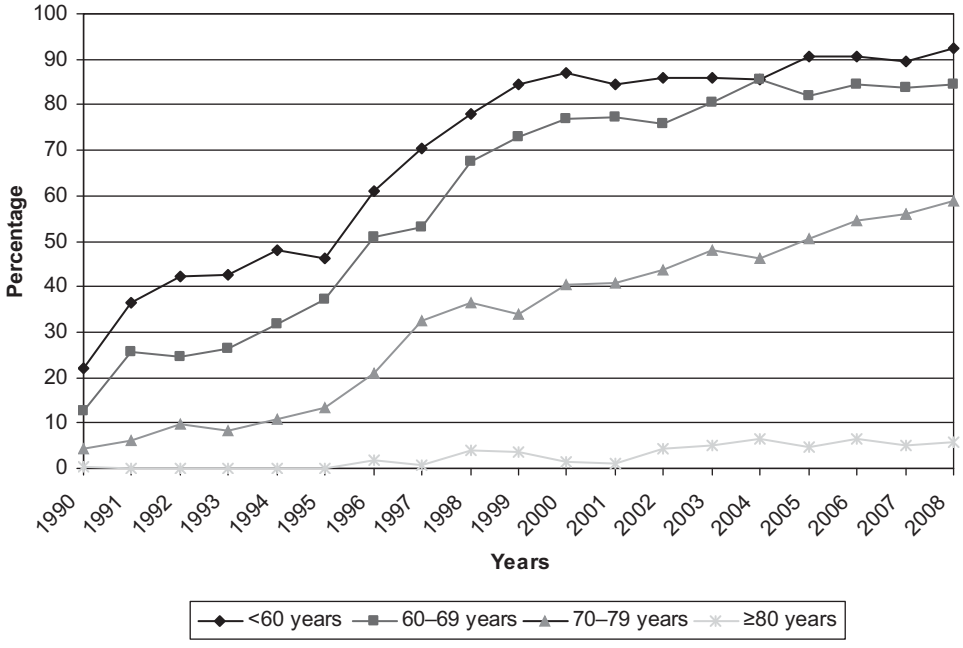
*Not otherwise specified and unknown location.

than 60 years; from 12.8% to 84.5% for patients aged 60 to 69 years; from 4.2% to 58.8% for patients aged 70 to 79 years; and from 0.5% to 5.6% for patients of 80 years and older ($p < 0.001$ for each age group, Figure 1). The odds of receiving adjuvant chemotherapy, adjusted for sex, age, anatomical location, differentiation, T-stage, N-stage, and hospital type, increased significantly in all age groups. The following factors were negatively associated with the administration of chemotherapy in younger patients (<70 years): increasing age, T4-stage, and tumours with unknown location. On the contrary, higher N-stage was associated with more frequent administration of adjuvant chemotherapy in younger patients. Patients aged 70 years or older received more frequently adjuvant chemotherapy with a higher N-stage, while in contrary, increasing age, female gender, and T4-stage were associated with less frequent administration of chemotherapy.

In 1990, less than 10% of all patients (all ages) received chemotherapy. As shown in Table II, a higher percentage of patients aged younger than 60 years were treated with adjuvant chemotherapy in 1990, and the percentage of patients receiving chemotherapy decreased with increasing age. In 1999 almost 50% of all patients received chemotherapy (all ages), which also decreased with increasing age. In both 1990 and 1999 patients were only treated with a combination of fluorouracil and folinic acid. In 2008 over 60% of all patients (all ages) received adjuvant chemotherapy. Since the guidelines have been revised in 2004 and 2008, patients in 2008 were treated more often with FOLFOX, CapOx (combination of capecitabine and oxaliplatin) or capecitabine as monotherapy (Table II). With increasing age, patients more often received capecitabine as a monotherapy and less often a combination of capecitabine with oxaliplatin or FOLFOX.

Costs of chemotherapy

Due to the low percentage of patients receiving chemotherapy in 1990 and the low costs for these chemotherapeutics (off patent), the costs were relatively low, €38 467 (Figure 2). The estimated costs per patient (total costs divided trough the number of patients treated) in 1990 were €459 for patients younger than 60 years, €445 for patients between 60 and 69 years, €427 for patients between 70 and 79 years, and €285 for patients 80 years and older,



Years of diagnosis	<60 years	60–69 years	70–79 years	≥80 years
OR over time*	1.23 (1.22–1.25)	1.22 (1.21–1.24)	1.19 (1.18–1.21)	1.17 (1.13–1.22)
(95%CI)				
p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**

*Adjusted for sex, age, grade, anatomical location, T-stage, N-stage, and hospital type.

Figure 1. Percentage of chemotherapy given per age group.

Table II. Type of chemotherapy in 1990, 1999, and 2008 per age group.

	No. of patients in 1990 (% of chemo)	No. of patients in 1999 (% of chemo)	No. of patients in 2008 (% of chemo)
Total no. of patients < 60 years	185	271	338
5-FU*	41 (22.2%)	229 (84.5%)	7 (2.0%)
FOLFOX-4	0 (0.0%)	0 (0.0%)	53 (15.7%)
CapOX	0 (0.0%)	0 (0.0%)	222 (65.7%)
Capecitabine mono	0 (0.0%)	0 (0.0%)	30 (8.9%)
Total no. of patients with chemotherapy	41 (22.2%)	229 (84.5%)	312 (92.3%)
Total no. of patients 60–69 years	251	322	504
5-FU*	32 (12.8%)	235 (73%)	10 (2.0%)
FOLFOX-4	0 (0.0%)	0 (0.0%)	72 (14.2%)
CapOX	0 (0.0%)	0 (0.0%)	276 (54.8%)
Capecitabine mono	0 (0.0%)	0 (0.0%)	68 (13.5%)
Total no. of patients with chemotherapy	32 (12.8%)	235 (73%)	426 (84.5%)
Total no. of patients 70–79 years	284	477	563
5-FU*	12 (4.2%)	162 (34%)	20 (3.5%)
FOLFOX-4	0 (0.0%)	0 (0.0%)	46 (8.2%)
CapOX	0 (0.0%)	0 (0.0%)	125 (22.2%)
Capecitabine mono	0 (0.0%)	0 (0.0%)	140 (24.9%)
Total no. of patients with chemotherapy	12 (4.2%)	162 (34%)	331 (58.8%)
Total no. of patients ≥ 80 years	190	271	357
5-FU*	1 (0.5%)	10 (3.7%)	4 (1.1%)
FOLFOX-4	0 (0.0%)	0 (0.0%)	0 (0.0%)
CapOX	0 (0.0%)	0 (0.0%)	4 (1.1%)
Capecitabine mono	0 (0.0%)	0 (0.0%)	12 (3.4%)
Total no. of patients with chemotherapy	1 (0.5%)	10 (3.7%)	20 (5.6%)
Total no. of patients in each year with chemotherapy	86 (9.5%)	636 (47.4%)	1089 (61.8%)

*5-FU in combination with folinic acid

as shown in Supplementary Attachment 1 (available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2012.739730). With increasing age, fewer patients completed six months of chemotherapy, resulting in lower costs per patient with increasing age. Guidelines of adjuvant chemotherapy were widely incorporated in 1999, as is shown in Figure 1. The costs for chemotherapy in the present dataset for 1999 were approximately €262 040. The estimated costs of chemotherapy per person were between €264 and €426 for the different age groups. In 2008, the costs of chemotherapy were higher due to the frequent use of capecitabine, an oral 5-fluorouracil analogue, which is still under a patent. Furthermore, oxaliplatin was widely incorporated as adjuvant chemotherapy in addition to fluorouracil and folinic acid (FOLFOX). The estimated costs per person in 2008 varied between €1933 and €3800 and total costs were estimated to be €3 876 150.

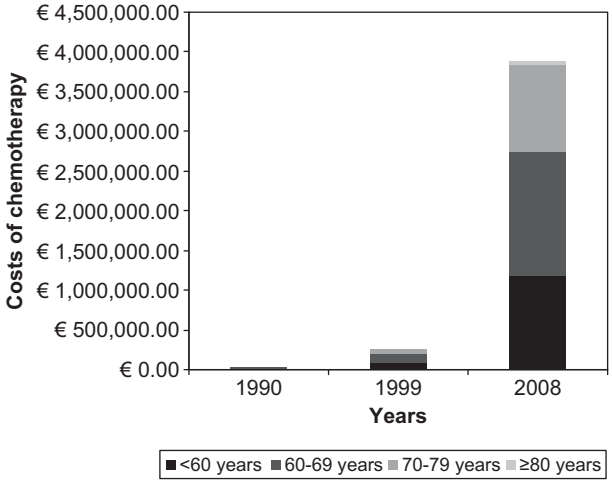
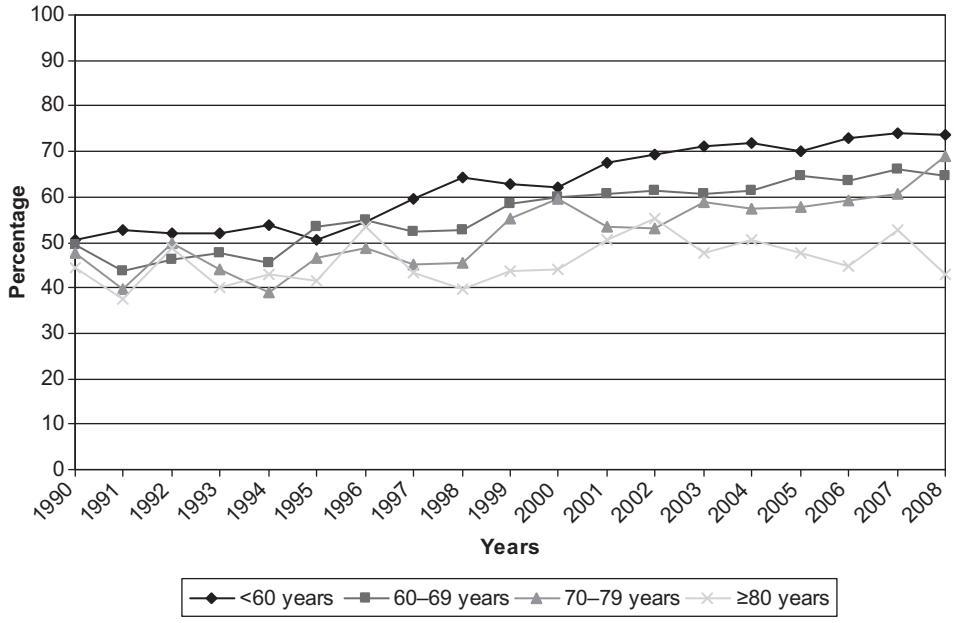


Figure 2. Changes of total costs of chemotherapy over time.

Survival

Five year overall survival for colon cancer patients with stage III increased over time from 38.7% in 1990–1996, to 45.9% in 1997–2002, and to 51.6% in 2003–2008 (HR over incidence periods = 0.82; 95% CI 0.80–0.84; $p < 0.001$). The five year relative survival increased from 47.3% in 1990–1996, to 55.3% in 1997–2002, and to 62.2% in 2003–2008 (RER over incidence periods = 0.96; 95% CI 0.96–0.97; $p < 0.001$, Figure 3). The improvement of relative survival was less pronounced with increasing age with a RER of 0.94 (95% CI 0.93–0.95; $p < 0.001$) for patients younger than 60 years, RER of 0.95 (95% CI 0.95–0.96; $p < 0.001$) for patients 60–70 years, RER of 0.96 (95% CI 0.95–0.97; $p < 0.001$) for patients between 70 and 80 years and



	Chemotherapy		No chemotherapy	
	RER (95%CI)	p-value	RER (95%CI)	p-value
<60years	0.93 (0.91–0.94)	**<0.001**	1.01 (1.00–1.03)	0.1
60–69years	0.94 (0.93–0.96)	**<0.001**	1.02 (1.00–1.03)	**0.01**
70–79years	0.92 (0.90–0.94)	**<0.001**	1.00 (0.99–1.00)	0.3
≥80years	0.83 (0.73–0.94)	**0.004**	0.98 (0.97–0.99)	**<0.001**

*Adjusted for sex, age, grade, anatomicallocation, T-stage, N-stage, and hospital type.

Figure 3. Relative survival over time per age group, with multivariable relative survival per age group in the table.

a RER of 0.99 (95% CI 0.98–1.00; $p = 0.01$) for patients of 80 years and older.

The multivariable relative survival analyses were adjusted for sex, age, grade, anatomical location, T-stage, N-stage, and hospital. The multivariable relative survival of patients receiving chemotherapy increased for each age group over time (table below Figure 3). However, the multivariable relative survival of patients not receiving chemotherapy was less consistent over time. Whereas the survival of patients aged 60 to 69 years who did not receive chemotherapy decreased over time, the survival of patients aged 80 years or older has improved over time. Relative survival of the other age groups not receiving chemotherapy remained stable over time. Of the patients that did not receive adjuvant chemotherapy, female patients had a better relative survival. Relative survival decreased with higher grade, T-stage, and N-stage in both the group of patients receiving adjuvant chemotherapy, as well as the group of patients not receiving adjuvant chemotherapy ($p < 0.001$).

Discussion

In this nationwide population-based study covering a period of 18 years, we showed that both administration of chemotherapy and survival of patients with stage III colon cancer increased during the study period. Whereas the administration of chemotherapy increased considerably during the period, survival increased to a lesser extent. New chemotherapeutics were introduced during the study period, which led, together with the increased use of chemotherapy, to increasing costs of chemotherapy per patient.

Administration of chemotherapy

The changes in administration of chemotherapy and survival of colon cancer found in this study are in line with earlier studies in The Netherlands and other European countries [13,14]. The results of randomised clinical trials published during the study period have been implemented in guidelines and

clinical practice, resulting in a large increase in the use of adjuvant chemotherapy. Our observation that elderly patients received chemotherapy less frequently as compared to younger patients is in line with previous studies [15,16]. There are several reasons why elderly patients are less likely to receive adjuvant chemotherapy; they include the presence of comorbidities, frailty, the absence of supportive caregivers, and a decrease in patients' general condition and cognitive ability [17]. In addition, elderly patients seem to be less willing to accept the negative side effects of chemotherapy, resulting in more frequent patient refusal, and some medical oncologists will probably offer the elderly less often adjuvant chemotherapy [18]. However, fit elderly colon cancer patients may benefit equally from adjuvant chemotherapy without increased toxicity [9,10]. Over time, patients were more often treated with FOLFOX, CapOx, or capecitabine monotherapy, according to the results of the MOSAIC trial, the NSABP C-07 trials, and the adjustments in the guidelines [6,8,19]. The addition of oxaliplatin showed an improved disease free survival for stage III colon cancer patients [6,19]. Since subgroups analyses of these two studies have shown that elderly patients with an age of 70 years and older are less likely to benefit from the addition of oxaliplatin, elderly patients in our study indeed received less often oxaliplatin in addition to oral fluorouracil with folinic acid, or in addition to capecitabine [20,21]. Furthermore, capecitabin monotherapy has been shown to be as least as effective as intravenous fluorouracil in combination with folinic acid [7].

Costs of chemotherapy

The costs of chemotherapy are expected to be an underestimation since only the costs for the medication, and no hospital or material costs, were included. Furthermore, patients who did not complete the chemotherapy were calculated to have had 50% of the expected chemotherapy costs, which also might have led to an underestimation. Despite these limitations, costs of chemotherapy have increased considerably during the study period, especially in the last period, due to the use of newer chemotherapeutics. Cost-effectiveness cannot be calculated with the design of this study. However, we observe high costs for the adjuvant chemotherapy (between €1933 and €3800 per person in 2008). Recently, Pandor et al. have shown in their systematic review that the use of oral fluorouracil is cost-effective, based on quality adjusted life years (QALYs) [22].

The end of the patent on oral fluorouracil, capecitabine, in December 2013, will probably result in lower costs per person. Furthermore, subset analyses of recent studies have shown that oxaliplatin might not be effective in elderly colon cancer patients [20,21], which could decrease the costs in the coming years.

Overall, the improvement in survival found in this study was accompanied by an approximately 100-fold increase in the costs of chemotherapy. Currently, the question is how much more costs can be accepted. The proportion between the improvement in survival and the increase in costs should be balanced. Perhaps, other ways to improve survival, such as peri-operative care or low-cost drugs such as aspirin [23], should be implemented first, since these improvements might be relatively cheap and less toxic in comparison to new chemotherapeutics.

Survival

The considerable improvement in five year relative survival of patients who received chemotherapy over time with 7% for patients younger than 60 years, 6% for patients between 60 and 69 years, 8% for patients between 70 and 79 years, and 17% for patients 80 years and older, is thought to be at least in part attributable to the increased use of adjuvant chemotherapy. Stage migration and improved peri-operative care probably played an additional role, although these data were not available. Although the percentage of patients receiving chemotherapy increased most for patients younger than 60 years and less with increasing age, elderly patients who did receive chemotherapy had the highest increase in relative survival, indicating differences in the selection of patients receiving chemotherapy within each age group.

In the adjuvant studies that demonstrated decreased colon cancer relapse and increased overall survival, the mean age was below 65 years and the small number of older patients does not allow firm conclusions to be drawn on the benefits of adjuvant therapy in elderly patients [10].

For patients not receiving adjuvant chemotherapy the relative survival remained almost stable, although there was an age disparity in time trends of relative survival. For patients aged younger than 80 years relative survival decreased or remained stable over time. The use of adjuvant therapy for these patients increased from approximately 10% to 80%. Hence, the selection of patients has changed over time from broad representation of unselected stage III patients who received no chemotherapy to a small group of highly selected patients for whom adjuvant therapy was not deemed beneficial for survival because of factors associated with an unfavourable outcome itself, such as comorbidities.

For patients aged 80 years and older, relative survival increased over time for both those who did and those who did not receive adjuvant chemotherapy. Improved survival might be due to increased life expectancy and improved peri-operative care. Besides, stage migration with improved detection of metastases during the preoperative work-up might have contributed as well [14,24]. However, we have to interpret these retrospective data with caution. Nevertheless, these patients deserve more attention and research regarding adjuvant treatment.

Strengths and limitations

This population-based study has some limitations. Firstly, it lacks details concerning emergency surgery and the presence of comorbidities. Both are associated with increased postoperative complications and mortality and reduced administration of chemotherapy. Elderly patients are more likely to undergo emergency surgery and also the incidence of comorbidity increases with age [25]. Secondly, the costs of chemotherapy and the number of patients completing chemotherapy per age group were estimated. Furthermore, the costs of complications and additional costs, such as material and hospital stay, were not taken into account. This probably resulted in an underestimation of the actual costs of chemotherapy.

Thirdly, stage migration probably played a role in the survival changes over time, as lymph node detection has improved and advanced diagnostic methods might have increased recognition of metastases [14,24]. It is unknown which part of the improvement in survival over time can be explained by stage migration, and which part can be attributed to changes in treatment.

Nevertheless, this study has several strengths. It is a large population-based study, which used stratification according to age groups with comparison between younger and elderly patients and the receipt of chemotherapy over a long period of time, so that time trends could be studied. Furthermore, this is the first study to present the absolute costs of chemotherapy for colon cancer patients in The Netherlands.

Conclusion

In conclusion, the administration of chemotherapy and costs increased considerably over time, although many elderly patients still do not receive adjuvant chemotherapy. The relative survival of patients receiving chemotherapy increased over time, while the relative survival of patients who did not receive chemotherapy remained almost stable. Although administration of chemotherapy increased considerably during the study period, relative survival increased to a lesser extent. In our study we show that elderly patients who did receive adjuvant chemotherapy have at least equal improvement in relative survival as compared to younger stage III colon cancer patients, suggesting that there are differences in the selection of patients receiving adjuvant chemotherapy in each age group. Furthermore, the current results show the importance of selecting patients for whom chemotherapy is expected to be beneficial.

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Supplementary material available online

Attachment 1