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Tumour stage and implementation of standardised cancer patient pathways:

a comparative cohort study

Abstract

Background
Some European countries have introduced standardised cancer patient pathways (CPPs), including urgent referrals, with the aim of diagnosing cancer at an earlier stage. This is despite a lack of evidence, particularly in patients with symptomatic cancer diagnosed via general practice.

Aim
To compare tumour stages in patients with incident cancer diagnosed via general practice before, during, and after CPP implementation in Denmark in 2008–2009.

Design and setting
A comparative cohort study of data from GPs and registries on patients with incident cancer listed with a GP before (n = 1420), during (n = 5272), and after (n = 2988) CPP implementation.

Method
χ^2 test was used to compare stage distributions and logistic regression to estimate odds ratios (OR) of having local cancer after versus before CPP implementation.

Results
Distribution of tumour stages did not differ statistically significantly across time (P = 0.494) or between CPP use (P = 0.202). For all cancers combined, the OR of having local cancer after CPP implementation was 0.88 (95% confidence interval [CI] = 0.73 to 1.06) compared with before. For CPP-referred patients, the OR of having local cancer was 0.77 (95% CI = 0.62 to 0.94) compared with all patients before CPP implementation; the corresponding OR for non-CPP-referred patients was 0.96 (95% CI = 0.80 to 1.14).

Conclusion
No clear tendencies were observed confirming earlier detection of cancer after rather than before CPP implementation. CPP-referred patients had lower odds of having local cancer after CPP implementation than all patients before CPP implementation; this could be because the GPs refer patients who are 'more ill' as urgent referrals.

Keywords
cancer; Denmark; early diagnosis; general practice; tumour stage; urgent referral.

INTRODUCTION

In recent years standardised cancer patient pathways (CPPs), including urgent referral, have been introduced in some European countries to accelerate diagnostic work.[1–9] Denmark implemented CPPs in 2008 and 2009.[2] The Danish CPPs consist of guidelines, including descriptions of selected alarm symptoms that may raise cancer suspicion, descriptions of medical procedures (mainly in the secondary healthcare sector), and specific timeframes for all phases (for example, 9 days from GP referral to first appointment at hospital when colorectal cancer is suspected).[2,10]

CPP strategies differ by country, but they tend generally to rest on the common assumption that improved prognosis (that is, better survival) can be ensured by shorter time to diagnosis and hence earlier detection of cancer. As survival is highly dependent on the tumour stage at diagnosis,[11–13] tumour stage is a fair proxy for prognosis.

Although >80% of patients with cancer are diagnosed via a general practice route,[14,15] the effect of CPP implementation on tumour stage has been evidenced in only three studies of patients diagnosed via a primary care route, and with conflicting results.[5,16,17] In cross-sectional studies, tumour stages seem to differ according to referral routes (CPP or not) for some cancer sites: more advanced stages for lung and ovarian cancer among those urgently referred, no difference for prostate cancer, and diverging results for colorectal cancer.[7,9,18–20] This could indicate that a selection is performed by the GP to comply with CPP guidelines.

The present study aimed to examine the effect of CPP implementation to identify tumours at earlier stages for seven different cancer types among symptomatic patients diagnosed via a general practice route. Furthermore, the study aimed to evaluate whether identified associations between CPP implementation and tumour stage may be interpreted as reflecting a causal relationship or whether results are biased by clinical decision making through a GP's use of CPP referral.

METHOD

Data from GPs and registries from the Danish Cancer in Primary Care (CaP) cohort[21] were used to compare tumour stage among patients with incident cancer diagnosed via a general practice route before, during, and after CPP implementation.

Setting

The study took place in Denmark, where the

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How this fits in

The effect of implementation of urgent referral schemes on tumour stage at diagnosis is unknown. This study found that implementation of urgent referrals (named cancer patient pathways [CPPs] in Danish) in Denmark was not associated with lower tumour stage and that urgently referred patients tended to have worse tumour stage than non-urgently referred patients. These findings can be explained by selection of a certain patient group for CPP referral and indicate that a narrow focus on a predefined checklist of specific symptoms and corresponding guidelines may lead to overlooking the double-sided nature of the clinical triage in general practice.

publicly funded healthcare system ensures free access to diagnostic procedures and treatment for all citizens. Almost all citizens (>98%) are registered with a specific general practice, which acts as gatekeeper to the rest of the healthcare system (except for otorhinolaryngologists and ophthalmologists who can be accessed directly).[22] A national screening programme for breast cancer was implemented in Denmark in 2007–2009, making patients with breast cancer ineligible for the present study. Patients with prostate cancer also were ineligible because of the increased use of prostate specific antigen (PSA) tests in general practice,[23] which, unrelated to CPP implementation, increased the proportion of localised tumours detected.[24,25]

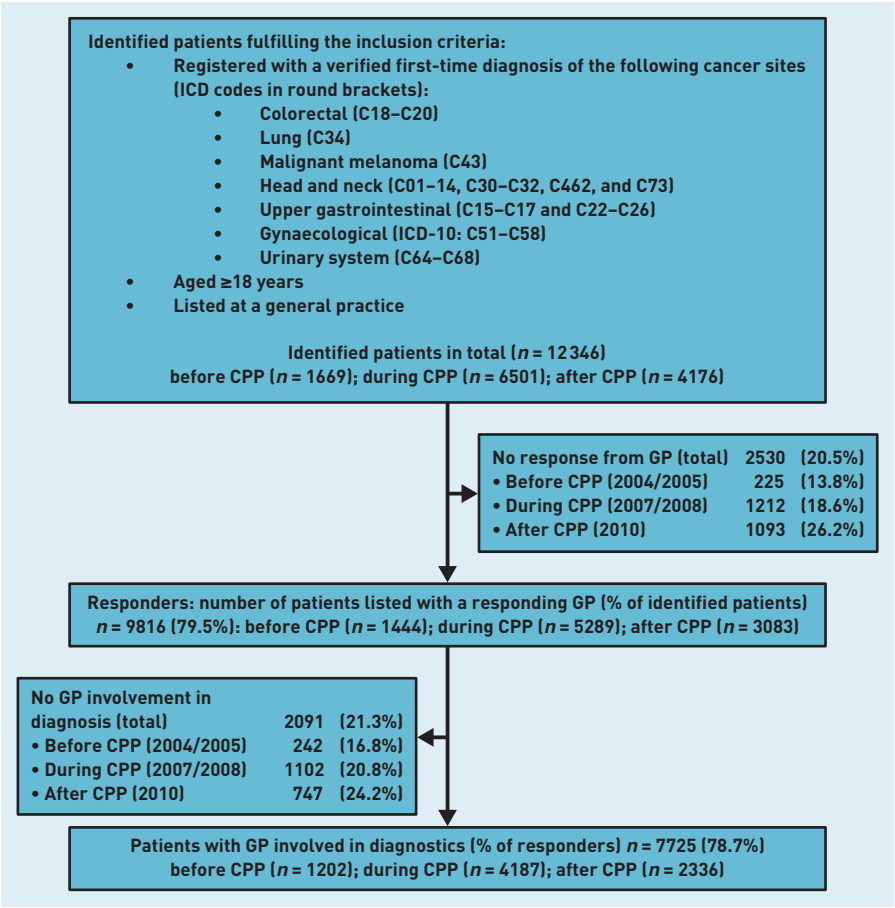


Figure 1. Flowchart showing patient identification, drop-out, and GP involvement. The box on the left indicates exclusion of patients because of no GP involvement, whereas the box on the right indicates drop-out because of GP non-response. CPP = cancer patient pathways. ICD = International Statistical Classification of Diseases and Related Health Problems.

Identification of patients and data collection

Patients were identified in hospital registers and in the Danish National Patient Registry before (1 September 2004 to 31 August 2005), during (1 October 2007 to 30 September 2008), and after (1 May 2010 to 31 August 2010) CPP implementation. Patients were eligible if they were aged ≥18 years, were listed with a GP, attended general practice as part of their diagnostic route, and were registered with a verified first-time diagnosis of colorectal cancer (ICD-10: C18– C20), lung cancer (ICD- 10: C34), malignant melanoma (ICD-10: C43), head and neck cancer (ICD-10: C01–14, C30–C32, C462, and C73), upper gastrointestinal (upper GI) cancer (ICD-10: C15–C17 and C22–C26), gynaecological cancer (ICD-10: C51–C58), or urinary system cancer (ICD-10: C64–C68). The GP's involvement was defined on the basis of the response (yes/no) to the following question in the GP questionnaire: 'Were you/your general practice involved in diagnosing the cancer?'[21]

Variables used in this study

Clinical tumour stage was obtained from the Danish Cancer Registry and was based on the TNM classification of malignant tumours (T = size of Tumour, N = involved lymph Nodes, M = distant Metastasis) staging system. Tumour stage was categorised for colorectal, lung, malignant melanoma, and bladder cancers using established cancer-specific algorithms to categorise tumours with missing TNM components as: local, regional, distant, unknown (partly missing TNM components), or missing (all TNM components missing).[26–29] TNM staging information for the remaining patients was categorised as local (no positive lymph nodes or metastasis), regional (positive lymph nodes), distant (metastatic cancer), missing (no T, N, and M information), or unknown (all remaining cancers).[21]

Exposure was the sampling time for the three sub-cohorts according to the CPP implementation: 2004/2005 = before CPP implementation (before), 2007/2008 = during CPP implementation (during), and

Table 1. Demographic characteristics of patients diagnosed through a primary care route; before, during, and after the implementation of cancer patient pathways. The 'after' cohort is also shown by referral route (*n* = 7725)

	Before		During transition		After							
					Total		CPP-referred		Non-CPP referred		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	1202	100	4187	100	2336	100	772	100	1564	100	7725	100
Sex												
Female	624	51.9	2120	50.6	1128	48.3	346	44.8	782	50.0	3872	50.1
Male	578	48.1	2067	49.4	1208	51.7	426	55.2	782	50.0	3853	49.9
Age groups, years												
18–44	84	7.0	258	6.2	141	6.0	39	5.1	102	6.5	483	6.3
45–54	138	11.5	469	11.2	264	11.3	73	9.5	191	12.2	871	11.3
55–64	293	24.4	1040	24.8	549	23.5	196	25.4	353	22.6	1882	24.4
65–74	337	28.0	1235	29.5	724	31.0	252	32.6	472	30.2	2296	29.7
≥75	350	29.1	1185	28.3	658	28.2	212	27.5	446	28.5	2193	28.4
Diagnosis												
Colorectal	283	23.5	1073	25.6	629	26.9	224	29.0	405	25.9	1985	25.7
Lung	280	23.3	1018	24.3	501	21.4	202	26.2	299	19.1	1799	23.3
Melanoma	125	10.4	403	9.6	236	10.1	82	10.6	154	9.8	764	9.9
Head and neck	74	6.2	260	6.2	180	7.7	39	5.1	141	9.0	514	6.7
Upper gastrointestinal	185	15.4	570	13.6	336	14.4	84	10.9	252	16.1	1091	14.1
Gynaecological	141	11.7	484	11.6	250	10.7	64	8.3	186	11.9	875	11.3
Urinary system	114	9.5	379	9.1	204	8.7	77	10.0	127	8.1	697	9.0
Comorbidity, CCI (index date = date of diagnosis)												
None	793	66.0	2913	69.6	1636	70.0	572	74.1	1064	68.0	5342	69.2
Moderate	319	26.5	1051	25.1	563	24.1	169	21.9	394	25.2	1933	25.0
High	90	7.5	223	5.3	137	5.9	31	4.0	106	6.8	450	5.8
Educational level, ISCED												
Low (1 + 2)	473	39.4	1874	44.8	897	38.4	310	40.2	587	37.5	3244	42.0
Medium (3 + 4)	421	35.0	1450	34.6	883	37.8	282	36.5	601	38.4	2754	35.7
High (5 + 6)	202	16.8	641	15.3	456	19.5	149	19.3	307	19.6	1299	16.8
Missing	106	8.8	222	5.3	100	4.3	31	4.0	69	4.4	428	5.5
Annual disposable income, OECD tertiles												
Lower	378	31.4	1323	31.6	778	33.3	273	35.4	505	32.3	2479	32.1
Medium	363	30.2	1364	32.6	802	34.3	260	33.7	542	34.7	2529	32.7
Higher	395	32.9	1360	32.5	753	32.2	239	31.0	514	32.9	2508	32.5
Missing	66	5.5	140	3.3	3	0.1	0	0	3	0.2	209	2.7

CCI = Charlson's Comorbidity Index. ISCED = International Standard Classification of Education. OECD = Organisation for Economic Co-operation and Development.

2010 = after CPP implementation (after). The 'after' group was subsequently categorised as 'CPP-referred patients' and 'non-CPP-referred patients' based on GP-reported information on referral route.[21]

Confounding effects were controlled for in categories of sex, comorbidity, educational level, and disposable income, and also age centred at 45 years; details are published elsewhere.[21]

Statistical analyses

Complete case analyses were performed. Differences in tumour stage distribution were compared using Pearson χ^2 test.

Tumour stage was dichotomised into local and regional/distant combined (unknown and missing tumour stage excluded). Logistic regression was used to estimate the odds ratios (OR) of having a local tumour stage after versus before CPP implementation. Two adjusted models were considered: one with no regard of referral route (overall trend) and another with CPP-exposed patients divided into referral routes (trend by referral route).

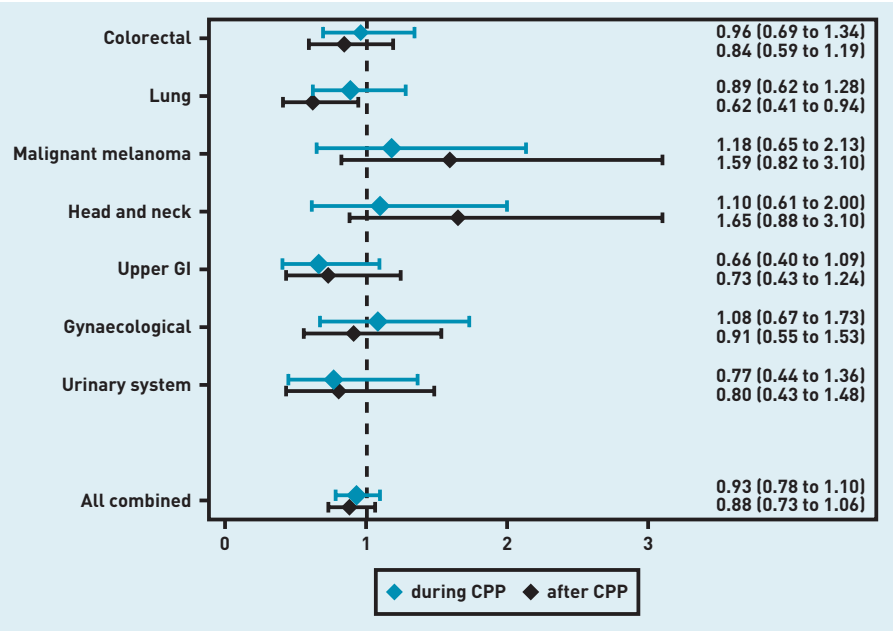


Figure 2. Odds ratios and 95% CIs for patients with incident cancer with non-missing tumour stage diagnosed through a primary care route having local cancer during (blue) and after (black) CPP implementation compared with before CPP implementation. Values <1 indicate less likelihood of having local cancer compared with before CPP implementation. All values are adjusted for sex, age, cancer site, comorbidity, educational level, and household income. GI = gastrointestinal.

Model fit was assessed by Pearson goodness-of-fit test.

The impact of selection bias and missing data of tumour stage was investigated by sub-analyses of all complete cases, regardless of whether general practice was involved or not, including patients with a non-participating GP (n = 9736) and by multiple imputation (n = 12 346). Multiple imputations were done by a multivariate model with 1-year survival, sex, age, comorbidity, income, educational background, and cancer site as predictors of missing and unknown tumour stage, missing educational level, and income.

Analyses were done using Stata statistical software (version 13), and a value of $P \leq 0.05$ was considered significant in all analyses.

RESULTS

Of 12 346 patients with incident cancer identified, GP responses were received for 9816 cases (79.5%) (Figure 1). Patients with participating GPs were less likely to be male and had fewer missing data on tumour stage than other patients (data not shown). The GPs reported being involved in diagnosing cancer for 7725 (78.7%) of the included cases. The study population is described in Table 1.

Overall tumour stage across time

The tumour stage distribution did not differ across time for all cancers combined (P = 0.494), nor for the individual cancer types (Table 2). Proportions of missing and unknown tumour stages differed statistically significantly, however, across time for all cancers combined (P<0.001) and for colorectal, lung, head and neck cancers, and gynaecological cancers (Table 2).

For all cancers combined, the OR of having local cancer was 0.88 (95% CI = 0.73 to 1.06) after CPP implementation compared with before (Figure 2). Patients with lung cancer had an OR of 0.62 (95% CI = 0.41 to 0.94) of having local cancer after CPP implementation compared with before (Figure 2). The ORs of having local cancer during CPP implementation compared with before were similar for all cancer types and for all cancers combined (Figure 2). The sensitivity analyses showed no changes in estimates for all patients (regardless of involvement of general practice), nor after multiple imputations (Appendices 1–3).

Tumour stage by referral route

The tumour stage distributions did not differ between CPP-referred and non-CPP-referred patients (Table 2). Yet, for all cancers combined, non-CPP-referred patients had higher proportions of unknown and missing tumour stages than CPP-referred patients (P = 0.006).

For all cancers combined, an OR of 0.77 (95% CI = 0.62 to 0.94) of having local cancer was identified for CPP-referred patients compared with the total group of patients before CPP implementation (Figure 3). Similar patterns were observed across different cancer types, but all 95% CIs of the ORs included 1 (Figure 3). For all cancers combined, CPP-referred patients tended to be less likely than non-CPP-referred patients to be diagnosed with localised

Table 2. Tumour stage distribution for patients diagnosed via a primary care route shown for seven cancer types and total

	Before		During		After			CPP-referred		Non-CPP-referred		
	n	%	*n*	%	*n*	%	*P*-value[a]	*n*	%	*n*	%	*P*-value[b]
Colorectal cancer (*n* = 1985)												
Local	86	30.4	340	29.0	201	32.0		71	31.7	130	32.1	
Regional	67	23.7	279	23.8	176	28.0		67	29.9	109	26.9	
Distant	63	22.3	245	29.4	166	26.4	0.874[c]	62	27.7	104	25.7	0.847[c]
Unknown	60	21.2	202	17.2	82	13.0		23	10.3	59	14.6	
Missing	7	2.5	7	0.6	4	0.6	0.003[d]	1	0.4	3	0.7	0.569[d]
Lung cancer (*n* = 1799)												
Local	51	18.2	184	18.1	68	13.6		27	13.4	41	13.7	
Regional	53	18.9	167	16.4	97	19.4		41	20.3	56	18.7	
Distant	149	53.2	630	61.9	322	64.3	0.055[c]	132	65.3	190	63.5	0.946[c]
Unknown	23	8.2	36	3.5	14	2.8		2	1.0	12	4.0	
Missing	4	1.4	1	0.1	0	0.0	<0.001[d]	0	0.0	0	0.0	0.244[d]
Malignant melanoma (*n* = 764)												
Local	84	67.2	277	68.7	175	74.2		60	73.2	115	74.7	
Regional	10	8.0	39	9.7	21	8.9		8	9.8	13	8.4	
Distant	9	7.2	15	3.7	7	3.0	0.319[c]	3	3.7	4	2.6	0.853[c]
Unknown	18	14.4	65	16.1	33	14.0		11	13.4	22	14.3	
Missing	4	3.2	7	1.7	0	0.0	0.159[d]	0	0.0	0	0.0	0.950[d]
Head and neck cancer (*n* = 514)												
Local	25	33.8	96	36.9	71	39.4		16	41.0	55	39.0	
Regional	38	51.4	130	50.0	65	36.1		18	46.2	47	33.3	
Distant	2	2.7	11	4.2	6	3.3	0.347[c]	1	2.6	5	3.5	0.704[c]
Unknown	2	2.7	18	6.9	37	20.6		4	10.3	33	23.4	
Missing	7	9.5	5	1.9	1	0.6	<0.001[d]	0	0.0	1	0.7	0.360[d]
Upper gastrointestinal cancer (*n* = 1091)												
Local	32	17.3	81	14.2	52	15.5		13	15.5	39	15.5	
Regional	32	17.3	124	21.8	63	18.8		19	22.6	44	17.5	
Distant	70	37.8	248	43.5	147	43.8	0.536[c]	35	41.7	112	44.4	0.623[c]
Unknown	43	23.2	108	18.9	72	21.4		17	20.2	55	21.8	
Missing	8	4.3	9	1.6	2	0.6	0.057[d]	0	0.0	2	0.8	0.782[d]
Gynaecological cancer (*n* = 875)												
Local	95	67.4	308	63.6	165	66.0		38	59.4	127	68.3	
Regional	17	12.1	48	9.9	24	9.6		10	15.6	14	7.5	
Distant	15	10.6	61	12.6	38	15.2	0.742[c]	11	17.2	27	14.5	0.136[c]
Unknown	8	5.7	59	12.2	22	8.8		4	6.3	18	9.7	
Missing	6	4.3	8	1.7	1	0.4	0.049[d]	1	1.6	0	0.0	0.108[d]
Urinary system cancer (*n* = 697)												
Local	79	69.3	244	64.4	136	66.7		47	61.0	89	70.1	
Regional	2	1.8	20	5.3	12	5.9		6	7.8	6	4.7	
Distant	22	19.3	84	22.2	33	16.2	0.241[c]	13	16.9	20	15.7	0.526[c]
Unknown	8	7.0	21	5.5	22	10.8		10	13.0	12	9.4	
Missing	3	2.6	10	2.6	1	0.5	0.084[d]	1	1.3	0	0.0	0.463[d]
All cancers (*n* = 7725)												
Local	452	37.6	1530	36.5	868	37.2		272	35.3	596	38.1	
Regional	219	18.2	807	19.3	458	19.6		168	21.8	289	18.5	
Distant	330	27.5	1294	30.9	719	30.8	0.494[c]	257	33.3	462	29.5	0.067[c]
Unknown	162	13.5	509	12.2	282	12.1		71	9.2	211	13.5	
Missing	39	3.2	47	1.1	9	0.4	<0.001[d]	3	0.4	6	0.4	0.006[d]

[a] Test for differences in tumour stage distribution across time. [b] Test for differences in tumour stage distribution between CPP-referred and non-CPP-referred patients.
[c] Missing and unknown stage excluded. [d] Missing and unknown stage included. CPP = cancer patient pathway.

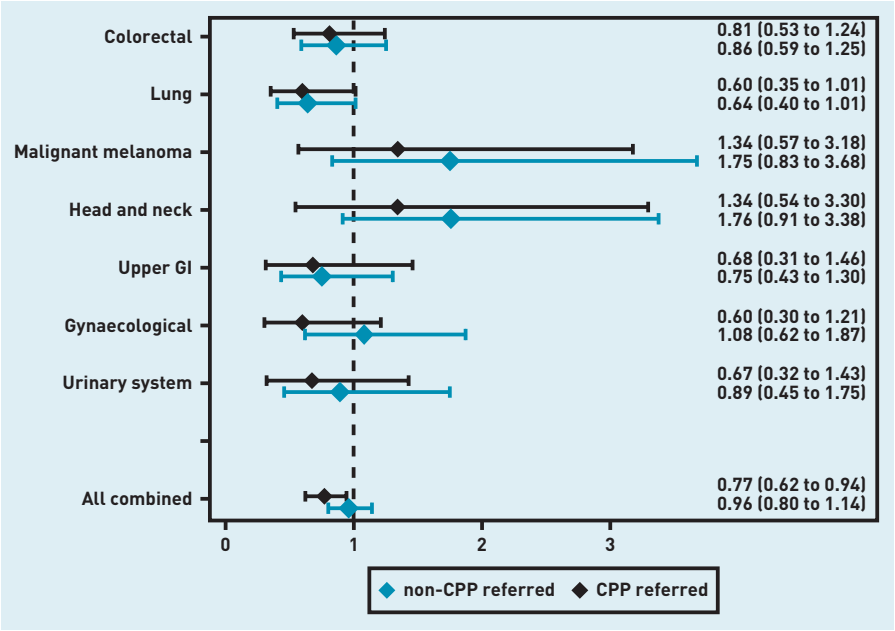


Figure 3. Odds ratios and 95% CIs for patients with incident cancer, with non-missing tumour stage diagnosed through a primary care route of having local cancer shown for CPP-referred patients (black) and non-CPP-referred patients (blue), both compared with all patients before CPP implementation. Values <1 indicate less likelihood of having local cancer compared with before CPP implementation. All values are adjusted for sex, age, cancer site, comorbidity, educational level, and household income. GI = gastrointestinal.

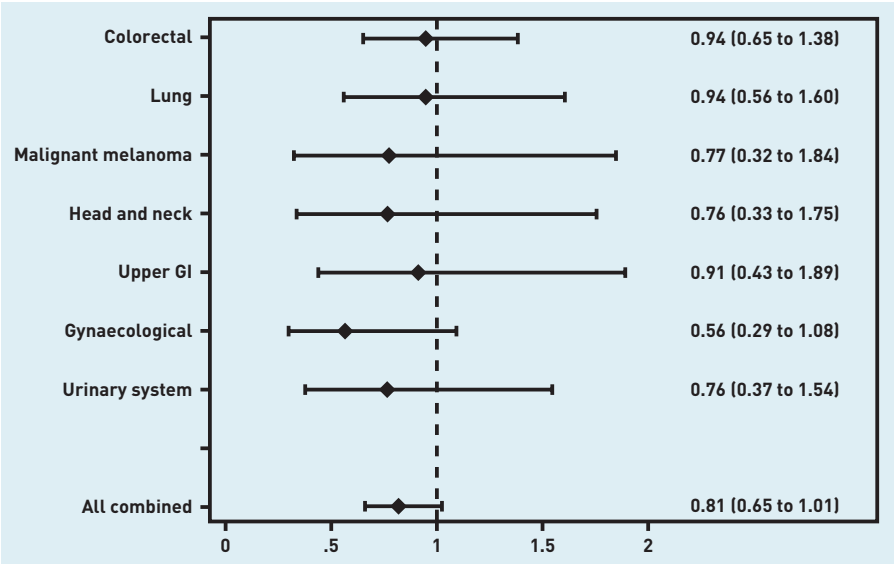
Figure 4. Odds ratios and 95% CIs of local cancer among CPP-referred patients compared with non-CPP-referred patients. Values <1 indicate that CPP-referred patients are less likely to have localised cancer than non-CPP-referred patients. All values are adjusted for sex, age, cancer site, comorbidity, educational level, and household income. GI = gastrointestinal.

cancer (OR 0.81, 95% CI = 0.65 to 1.01, *P* = 0.066) (Figure 4).

DISCUSSION

Summary

As the purpose of CPPs is to improve the prognosis of patients with cancer, a more favourable distribution of tumour stage after CPP implementation is anticipated. Yet, the present study found no evidence of a higher likelihood of having local cancer across time for all cancers combined for all patients with cancer, nor for patients diagnosed through general practice. Yet, the proportion of missing recordings of tumour stage decreased over time; this could indicate more complete staging and more complete records of staging information.



CPP-referred patients generally had a lower likelihood of having local cancer after CPP implementation compared with all patients before CPP implementation. CPP-referred patients also tended to be less likely to have local cancer than non-CPP-referred patients.

The results are likely to reflect more complete registration of tumour stage, stage migration, lack of statistical precision, and confounding by severity.

Strengths and limitations

The collective impact of CPP implementation was analysed, with emphasis on the case-mix of diagnoses, that is, variations across administrative time and space. Even though this study focused on patients diagnosed through general practice, the discussed methodological issues also refer to the analyses comparing all patients (Appendices 1–3).

The study design does not permit inference of causality, but it carries a risk that the association found between CPP implementation and localised tumour stage is coincidental. Furthermore, the study design cautions that the findings of more advanced tumours among non-CPP-referred patients cannot be rigorously interpreted as a causal effect of CPPs with the potential to disadvantage this group.

Selection bias was reduced during the identification of patients as all patients with cancer were included, regardless of symptom and cancer site, even late-registered patients.[9,20] Furthermore, the high response rate of 79% reduced the risk of selection bias. Although selection bias cannot be ruled out entirely, its role in this study seems to be minor as the sensitivity analyses displayed similar results.

The quality of available information may have changed over the study period because of clinical practice, increased intensity of investments, and modernisation of the Danish Cancer Registry (DCR) (from paper to electronic registration).[30,31] These changes may have biased the observed tumour stage across time. Incomplete staging information decreased over time, which may indicate improvements in staging and data-recording practices. Yet, missing data of tumour stages in the DCR is a well-known concern.[26–29,32] The present sensitivity analyses displayed identical results, however, which suggest that this potential bias alone cannot explain the findings.

Misclassification of tumour stages may have occurred in the present study for three reasons: data entry errors in the DCR,

misclassification of tumours (local, regional, or distant), and registration time of tumour stage (at diagnosis or at treatment start). It is believed that the potential misclassification of stages is non-differential and thus would tend to underestimate the associations found across time. Although bias related to registration time and data entry errors may be differentiated across time, it is believed that it may have led to underestimation of the ORs presented.

The confidence intervals were comparatively large (0.73 to 1.06), indicating that the non-significant findings may be a result of low statistical precision, although the observed OR of having local cancer was 0.88.

Slightly more distant/metastatic cancers were found in this study than those reported by the clinical databases of the Danish Multidisciplinary Cancer Groups (DMCGs) for colorectal, lung, and ovarian cancers during 2000–2012,[33] which calls into question the quality of TNM staging in the DCR.

Comparison with existing literature

Three former studies have compared tumour stage across time among patients diagnosed through a general practice route during CPP implementation, but these were restricted to include only highly selected groups of patients with two cancer types.[5,16,17] The results of no difference in tumour stages among patients with colorectal cancer are in line with the study by Zafar and colleagues.[17] The present findings contrast, however, the findings of more stage IV head and neck cancers reported by Lyhne and colleagues[5] and of more Dukes' stage A colorectal cancers reported by Cerdán-Santacruz and colleagues.[16]

No previous studies were found of patients with lung cancer diagnosed through a primary care route that compared tumour stages before and after CPP implementation. As the Danish CPP guidelines recommended intensified and better quality in the diagnostic work-up,[2] this may have directed a shift towards more thorough pre-therapeutic assessment, which could lead to more severely staged tumours at the time of diagnosis after CPP implementation.

Recent evidence has shown that malignant melanoma was more likely to be diagnosed as stage I cancer during 2009–2011 compared with 2004–2008.[34] This could be because of greater awareness mediated by a large national skin cancer campaign launched in 2007.[34]

It is believed that the finding that CPP-referred patients tend to be less likely to have local cancer than non-CPP-referred patients mainly reflects confounding by severity, that is, bias stemming from the inherent differences in prognosis given the severity of the patient's disease.[35] Clearly, the chance of being referred to CPP increases as the underlying disease evolves and produces more severe symptoms.[36] This may also be why tumour stages tend to differ according to referral routes (CPP or not) in other studies,[7,9,18–20] may explain why GPs select the most severely ill cases for CPP referral,[37] and may explain why the patients referred and diagnosed within the 2-week wait framework had higher tumour stage than other patients.[38] Therefore, the level of disease may in itself be a confounder and thus may constitute an unacknowledged methodological problem, which challenges testing the effect of CPP implementation on earlier detection of cancer in symptomatic patients.

Implications for research and practice

The possibility that part of the findings can be explained by confounding by severity, which originates from the selection of certain patient groups who are referred to the CPP route, indicates that a narrow focus on a predefined checklist of specific symptoms and corresponding guidelines may lead to disregarding the double-sided nature of the clinical triage in general practice: the GP is expected to spot (and refer) the seriously ill patients, but the GP is also expected to prevent healthy people from getting unnecessary examinations at hospitals.[39]

The double-sided nature of the clinical triage stresses the need for faster diagnostic work-up for patients who are not eligible for CPP referral. The introduction of CPPs allows the GPs to refer the most ill patients, but these patients may not profit the most in terms of earlier cancer stage from faster diagnosis. Furthermore, the present findings that the GPs refer the most ill patients to the CPPs (in line with the guidelines) and stage migration over time may indicate that tumour stage is an insufficient measure to evaluate the effectiveness of CPPs in an observational study design that spans many years. Even though no improvement in tumour stage was observed in this study, patients with symptomatic cancer may still benefit from more timely diagnosis in terms of less morbidity, better performance scores, and increased patient satisfaction. This needs to be tested in future studies.

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Ethical approval

The study was approved by the Danish Data Protection Agency (rec. no. 2009–41–3471). The Danish National Board of Health (now: the Danish Patient Safety Authority) gave permission to obtain information from the GPs' medical records without patient consent. According to the committee on health research ethics in the Central Denmark Region, no ethical approval was needed for the study.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

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Appendix 1. Tumour stages before, during, and after CPP implementation for all identified patients

	Before		During		After		Total		
	n	%	*n*	%	*n*	%	*n*	%	*P*-value
Colorectal cancer (*n* = 3067)									
Local	109	28.8	520	31.7	339	32.3	968	31.6	
Regional	84	22.2	402	24.5	266	25.4	752	24.5	
Distant	80	21.1	381	23.2	265	25.3	726	23.7	0.981[a]
Unknown	87	23.0	315	19.2	171	16.3	573	18.7	
Missing	19	5.0	22	1.3	7	0.7	48	1.6	<0.001[b]
Lung cancer (*n* = 3038)									
Local	84	20.5	298	18.5	171	16.8	553	18.2	
Regional	76	18.5	277	17.2	198	19.5	551	18.1	
Distant	203	49.5	958	59.4	607	59.7	1768	58.2	0.068[a]
Unknown	36	8.8	76	4.7	40	3.9	152	5.0	
Missing	11	2.7	3	0.2	0	0.0	14	0.5	<0.001[b]
Malignant melanoma (*n* = 1137)									
Local	99	61.5	408	68.7	287	75.1	794	69.8	
Regional	12	7.5	56	9.4	30	7.9	98	8.6	
Distant	13	8.1	24	4.0	15	3.9	52	4.6	0.085[a]
Unknown	21	13.0	90	15.2	50	13.1	161	14.2	
Missing	16	9.9	16	2.7	0	0.0	32	2.8	<0.001[b]
Head and neck cancer (*n* = 951)									
Local	49	37.1	217	46.8	144	40.6	410	43.1	
Regional	53	40.2	187	40.3	120	33.8	360	37.9	
Distant	5	3.8	23	5.0	13	3.7	41	4.3	0.820[a]
Unknown	5	3.8	28	6.0	75	21.1	108	11.4	
Missing	20	15.2	9	1.9	3	0.8	32	3.4	<0.001[b]
Upper gastrointestinal cancer (*n* = 1767)									
Local	43	17.0	124	13.7	106	17.3	273	15.4	
Regional	43	17.0	192	21.3	105	17.2	340	19.2	
Distant	82	32.4	363	40.2	253	41.4	698	39.5	0.060[a]
Unknown	69	27.3	209	23.1	140	22.9	418	23.7	
Missing	16	6.3	15	1.7	7	1.1	38	2.2	<0.001[b]
Gynaecological cancer (*n* = 1279)									
Local	117	64.3	423	60.6	250	62.7	790	61.8	
Regional	17	9.3	69	9.9	36	9.0	122	9.5	
Distant	24	13.2	104	14.9	70	17.5	198	15.5	0.733[a]
Unknown	11	6.0	89	12.8	40	10.0	140	10.9	
Missing	13	7.1	13	1.9	3	0.8	29	2.3	<0.001[b]
Urinary system cancer (*n* = 1107)									
Local	99	65.1	387	65.6	243	66.6	729	65.9	
Regional	3	2.0	25	4.2	20	5.5	48	4.3	
Distant	27	17.8	121	20.5	59	16.2	207	18.7	0.274[a]
Unknown	11	7.2	41	6.9	40	11.0	92	8.3	
Missing	12	7.9	16	2.7	3	0.8	31	2.8	<0.001[b]
Total (*n* = 12 346)									
Local	600	35.6	2377	36.6	1540	36.9	4517	36.6	
Regional	288	17.3	1208	18.6	775	18.6	2271	18.4	
Distant	434	26.0	1974	30.4	1282	30.7	3690	29.9	0.364[a]
Unknown	240	14.4	848	13.0	556	13.3	1644	13.3	
Missing	107	6.4	94	1.5	23	0.6	224	1.8	<0.001[b]

[a]Missing and unknown data excluded. [b]Missing and unknown data included. CPP = cancer patient pathway.

Appendix 2. Odds ratios and 95% CIs for patients with incident cancer, regardless of GP questionnaire response, of having local cancer during and after CPP implementation compared with before CPP implementation. Values <1 indicate less likelihood of having local cancer compared with before CPP implementation

	During				After			
	Raw		Adjusted		Raw		Adjusted	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Colorectal	1.00	0.77 to 1.30	0.98	0.73 to 1.31	0.96	0.73 to 1.27	0.92	0.68 to 1.24
Lung	0.80	0.61 to 1.05	0.80	0.60 to 1.08	**0.71**	0.53 to 0.95	**0.69**	0.51 to 0.94
Malignant melanoma	1.29	0.78 to 2.12	1.19	0.70 to 2.03	1.61	0.94 to 2.76	1.55	0.87 to 2.77
Head and neck	1.22	0.80 to 1.87	1.25	0.80 to 1.97	1.28	0.82 to 2.00	1.41	0.88 to 2.26
Upper gastrointestinal	0.65	0.44 to 0.97	0.62	0.41 to 0.95	0.86	0.57 to 1.30	0.81	0.53 to 1.25
Gynaecological	0.86	0.58 to 1.27	0.89	0.59 to 1.36	0.83	0.54 to 1.26	0.85	0.54 to 1.32
Urinary system	0.80	0.51 to 1.26	0.80	0.48 to 1.33	0.93	0.58 to 1.51	0.80	0.47 to 1.37
Total	0.90	0.80 to 1.01	0.90	0.77 to 1.04	0.90	0.79 to 1.02	0.90	0.77 to 1.05

Adjusted for sex, age, cancer site, comorbidity, educational level, and household income. CPP = cancer patient pathway. OR = odds ratio. Estimates marked by bold indicate statistically significant at P<0.05 level.

Appendix 3. Odds ratios and 95% CIs after multiple imputation for identified patients with incident cancer of having local cancer during and after CPP implementation compared with before CPP implementation. Values <1 indicate less likelihood of having local cancer compared with before CPP implementation

	During				After			
	Raw		Adjusted		Raw		Adjusted	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Colorectal	1.02	0.78 to 1.33	1.02	0.78 to 1.34	0.96	0.72 to 1.29	0.96	0.72 to 1.29
Lung	0.79	0.61 to 1.03	0.81	0.62 to 1.06	**0.70**	0.52 to 0.93	**0.70**	0.53 to 0.94
Malignant melanoma	1.25	0.77 to 2.04	1.25	0.76 to 2.04	1.57	0.92 to 2.68	1.55	0.90 to 2.67
Head and neck	1.21	0.78 to 1.88	1.25	0.80 to 1.95	1.26	0.80 to 2.68	1.29	0.81 to 2.05
Upper GI	0.58	0.39 to 0.87	0.59	0.39 to 0.89	0.79	0.53 to 1.18	0.81	0.53 to 1.22
Gynaecological	0.84	0.57 to 1.23	0.84	0.57 to 1.23	0.83	0.55 to 1.25	0.83	0.55 to 1.25
Urinary system	0.80	0.52 to 1.24	0.82	0.53 to 1.29	0.90	0.56 to 1.44	0.88	0.54 to 1.42
Total	0.90	0.80 to 1.02	0.88	0.77 to 1.02	0.91	0.79 to 1.03	0.91	0.78 to 1.06

Adjusted for sex, age, cancer site, comorbidity, educational level, and household income. CPP = cancer patient pathway. OR = odds ratio. Estimates marked by bold indicate statistically significant at P<0.05 level.