



Cancer diagnostic delays and travel distance to health services: A nationwide cohort study in Denmark

Line Flytkjær Virgilsen^{a,*}, Henrik Møller^{a,b,c}, Peter Vedsted^a

^a Research Unit for General Practice, Research Centre for Cancer Diagnosis in Primary Care (CaP), Department of Public Health, Aarhus University, Bartholins Allé 2, 8000, Aarhus C, Denmark

^b The Danish Clinical Registries (RKKP), Olof Palmes Allé 15, 8200, Aarhus N, Denmark

^c Cancer Epidemiology & Population Health, King's College London, Strand, London, WC2R 2LS, UK



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ABSTRACT

Background: This study aims to investigate the association between distance to health services and intervals in the cancer diagnostic pathway, and explore whether the diagnostic difficulty of the cancer influences this association.

Method: A nationwide cohort study was conducted based on data from both questionnaires and registries. Danish cancer patients diagnosed in 2005–2016 and their general practitioner (GP) were included if enrolled in the Danish Cancer in Primary Care (CaP) cohort ($n = 37,872$). The CaP cohorts provided data on intervals assessed by patients and GPs. The Geographical Information System (GIS) was used to calculate travel distances from the residence of the patient to their GP surgery and to the hospital of diagnosis.

Results: Longer travel distance to the hospital of diagnosis was associated with longer diagnostic interval. This association was strongest in the period before the implementation of Cancer Patient Pathways (CPP) in 2010. Patients with a cancer categorised as ‘hard to diagnose’ contributed mostly to the association. Longer travel distance to the GP was associated with shorter patient interval and primary care interval for patients diagnosed with cancer types ‘intermediate to diagnose’.

Conclusion: Travel distance to cancer diagnostic health care services was associated with interval length in the diagnostic pathway. This association was less pronounced in the period after introducing CPPs and also strongly depending of the underlying cancer type and symptomatology.

1. Introduction

Early diagnosis is important for cancer prognosis [1–3], and equal and easy access to health care is a priority in most Western health care systems [4,5]. The increasing centralisation in many health care systems could have conflicting effects; it enhances and stimulates specialised health services [6,7] and yet limits the access to health care [8,9]. This holds a risk of delays in the diagnosis of cancer and treatment initiation. Studies have reported on the association between travel distance and cancer prognosis [10–15] yet more knowledge is needed on the influence of travel distance on cancer outcome [9].

The distance from the patient's home address to the general practitioner (GP) could be associated with the time from the first symptom to help-seeking (i.e. the patient interval) [16]. One study found that long travel distance to the location of the first health care consultation was associated with longer patient interval [17]. Lower referral

propensities among GPs in remote geographical locations have been observed [18], but no studies have examined the association between travel distance to health services and the period from first GP consultation until referral (i.e. the primary care interval). Studies in this area have been called for [15] because the diagnostic journey usually begins in primary care [19,20]. Further, patients with long travel distance to hospitals may experience barriers to investigations [21,22]. Three studies have found an association between distance and secondary care or treatment intervals [17,23,24]. To our knowledge, none has investigated the time from presentation until diagnosis (i.e. the diagnostic interval).

The association between travel distance and cancer outcome is not straightforward [15,23]. It could be hypothesised that the diagnostic difficulty of the cancer [25], which is influenced by different symptomologies, could affect the GP's propensity to refer [26,27] in patients with longer distance, and thereby lead to prolonged intervals.

* Corresponding author.

E-mail address: line.virgilsen@ph.au.dk (L. Flytkjær Virgilsen).

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This study aims to investigate the association between travel distance from the patient's home to the GP and length of *patient interval* and *primary care interval*. The study also aims to investigate the association between travel distance from the patient's home to the hospital of diagnosis and length of *primary care interval* and *diagnostic interval*. Finally, the study aims to examine if an identified association is modified by the diagnostic difficulty of the cancer.

2. Methods

2.1. Setting

Denmark has a population of 5.7 million inhabitants and a population density of 129 per square mile. The health care system is tax-funded and provides free access to most health care services. Danish GPs serve as gatekeepers to the health care system [28]. GPs are the first point of contact and may refer their patients to specialised diagnostic investigation at hospital or specialised private practices for e.g. dermatologists or gynaecologists. Diagnostics of cancer at the hospitals depends on the specific cancer types, yet most specialised investigations (e.g. radiological investigations or endoscopies) are performed only at larger hospitals. If cancer is suspected, patients are typically enrolled in a Cancer Patient Pathways (CPP) which were implemented in Denmark during 2008–2010 to ensure fast investigation of patients with symptoms suggestive of cancer [29,30].

The hospital services have been organised in five administrative regions in Denmark since 2007 [4].

2.2. Design, study population and data collection

We conducted a population-based cohort study based on incident cancer patients [31] included in the Danish Cancer in Primary Care (CaP) cohorts. The CaP cohorts comprise six separate cohorts of cancer patients and their GPs (Table 1) and include 37,872 incident cancer cases. Patients were included if aged 18 years or older at diagnosis, listed with a GP, and diagnosed between 2005 and 2016. For all six cohorts, patients were identified through the Danish National Patient Register (DNPR) [32]. Patients received a postal questionnaire approximately three months after diagnosis if they were alive and not listed in the Danish Civil Registration System as unavailable for research studies. Through the Danish National Health Service Register [33], the GP of each patient was identified and invited to respond to a questionnaire about the diagnostic process of their patient. GPs of the patients who had deceased at the time of the data collection also received a questionnaire. The response rate was 52–70% for the patient questionnaire and 72–86% for the GP questionnaire (Table 1). All data used in this study was linked through the patient's unique civil registration number (CRN) [34].

Table 1

Key components of the six CaP Cohorts.

Cohort	CaP 1	CaP 2	CaP 3	CaP 4	CaP 5	CaP 6
Year of diagnosis	2005 ^a	2007–2008	2010	2010–2011	2013	2016
Age group included	≥ 18 years	≥ 18 years	≥ 18 years	≥ 18 years	≥ 40 years	30–99 years
Diagnosis included	ICD-10: DC00-DC96 ex.C44	ICD-10: DC00-DC96 ex.C44	ICD-10: DC00-DC96 ex.C44	Lung and CRC	Lunge, CRC, female breast and ovarian	ICD-10: DC00-DC96 ex.C44
Eligible patients*	N = 1629 ^a	N = 11429	N = 8199	N = 2,860	N = 1,889	N = 11,866
Response rates for patient and GP**	Patient: 53% GP: 86 %	Patient: 63% GP: 81%	Patient: 64% GP: 74%	Patient: N/A GP: 74%	Patient: 70% GP: 60 %	Patient: 52% GP: 72%

^a Sub-cohort 1 originally included patients diagnosed from September 2004, thus eligible patients in this cohort consisted of 2850 [31]. This study only included patients diagnosed from 1 January 2005 (N = 1629).

* Patients with a validated first-time diagnosis in the DCR or the DNPR and listed with a GP.

** Response rates for the patient questionnaires were calculated for contacted patients alive and not registered in the Civil Registration System with a standing rejection to be contacted for research purposes.

2.3. Time intervals

The CaP cohorts hold information on the time from first symptom recognition until initiation of treatment based on responses from patients and GPs defined according to the Aarhus Statement [16]. This study includes the patient interval (the time from first symptom recognition until presentation in general practice), the primary care interval (the time from first GP presentation until first GP referral), and the diagnostic interval (the time between first presentation until diagnosis).

The calculation of the intervals adhered to the following coding rules. For the patient interval, we used the dates reported by the patient. When this information was missing, dates assessed by the GP were used. The primary care interval and the diagnostic interval were calculated based on GP-reported dates. When this information was missing, dates assessed by the patient were used. The date of diagnosis was collected from the Danish Cancer Register [35] and used for calculation of the diagnostic interval. Previous studies have shown acceptable agreement between patient- and GP-assessed milestone dates in the diagnostic pathway [36].

2.4. Travel distance to health services

We applied the geographical software programme ArcGIS Network Analyst [37] to calculate the travel distance from the residence of the patients at the time of diagnosis to the health services, including (1) the address of the GP and (2) the address of the hospital where the patient was diagnosed. The hospital of diagnosis was identified based on registrations in the DNPR, where the entire hospital discharge history of the Danish population is recorded [32]. Using the Danish road network, we calculated the shortest road distances from the residence of each patient to the GP and to the hospital.

In the study population, it was possible to calculate distance to the GP for 35,408 (93.5%) patients and to the hospital of diagnosis for 36,241 (95.7%) patients.

2.5. Diagnostic difficulty group

To study if the association between travel distance to the health services and length of intervals was modified by the diagnostic difficulty of the cancer, patients were stratified into three levels of diagnostic difficulty based on the underlying cancer type: *easy*, *intermediate*, and *hard*. This categorisation was developed based on previous work categorising cancer types based on the positive predictive value of a symptom being cancer when presented in general practice [25–27]. The included cancer types are presented in Box 1. Cancer types not mentioned here (n = 3545) were not included in these sub-analyses.

Box 1

Diagnostic difficulty group based on cancer type including ICD-10 codes.

Easy (n = 12,416)		Intermediate (n = 12,511)		Hard (n = 9400)	
Rectal	(C19-20)	Oropharyngeal	(C10)	Stomach	(C16)
Melanoma*	(C43)	Oesophagus	(C15)	Pancreas	(C25)
Breast	(C50)	Colon	(C18)	Lung	(C34)
Vaginal	(C52)	Laryngeal	(C32)	Ovarian	(C56)
Cervical	(C53)	Mesothelioma	(C45-46)	Brain/CNS***	(C70-72)
Endometrial	(C54-55)	Vulva	(C51)	Hodgkin's Lymphoma	(C81)
Penile	(C60)	Prostate	(C61)	Multiple myeloma	(C90)
Testicular	(C62)	Renal	(C64)		
Bladder	(C67)	NH Lymphoma**	(C82,83,85)		
Thyroid	(C74-75)	Leukemia	(C91-C95)		

* Malignant melanoma
** Non-Hodgkin's Lymphoma
*** CNS: central nervous system

2.6. Covariates

The following variables were included as covariates and obtained from Statistics Denmark: sex, age at date of diagnosis (categorised into: 18–49, 50–59, 60–69, 70–79, and ≥ 80 years of age), and highest attained education (categorised according to UNESCO's ISCED classification into: ≤ 10 , 11–15, or > 15 years of education) [38]. Charlson's Comorbidity Index score was also included as a potential covariate and was assessed based on contacts registered in the DNPR ten years prior to the diagnosis (categorised into: 0, 1–2, > 2). Finally, we adjusted for sub-cohort to account for historic time and developments in diagnostic procedures over time.

2.7. Statistical analysis

Median and interquartile range (IQR) across SEP, distance, diagnostic difficulty groups, and period (before or after the introduction of CPPs) was assessed for the patient interval, the primary care interval, and the diagnostic interval. To test differences between groups, non-parametric tests (linear trend among ordered groups [39], Mann-Whitney Test, and Kruskal-Wallis test) were used.

To investigate the association between travel distance and intervals using continuous data, linear regression models were applied to predict the studied intervals as a function of distance to either the GP or the hospital. Prior to analyses, negative intervals were set at 0 days, and intervals of more than one year were truncated to 365 days in accordance with the coding rules by the International Cancer Benchmarking Partnership (ICBP) Module 4 [40].

Each association was estimated univariately and followed by a second model adjusting for age, sex, education, CCI, and sub-cohort. Identical analyses were then performed for the three diagnostic difficulty groups (easy, intermediate, and hard) for both travel distance to the GP and to the hospital of diagnosis which is presented in separate graphs due to large differences in the distribution of distance to the GP and distance to the hospital. E.g. 95% of the population lived within 12 km of their GP whereas 95% of the population lived within 85 km of the hospital. As the unadjusted and adjusted analyses were almost identical, only the adjusted results are shown. Finally, a stratified analysis was conducted to separate the period up to 2009 and the period from 2010 onwards. This was done to assess if the observed association was altered over a period during which several organisational changes were implemented in the Danish health care system.

All statistical analyses were performed using Stata software, version 15.0.

2.8. Ethics

The project is registered in the Record of Processing Activities at the Research Unit for General Practice in accordance with the Danish data protection regulations (L68) and the General Data Protection Regulation (GDPR) by the EU [41]. As the data is based solely on registry and questionnaire data, approval by the regional committee on health research ethics was not required.

3. Results

Table 2 shows that the median patient intervals were longer in patients who were younger, highly educated, a CCI score of 0, and in the period after CPP introduction. The median primary care intervals were longer in patients who were older, males, had short education, were hard to diagnose, and in the period before CPP introduction. The median diagnostic intervals were longer in patients who were oldest, males, a CCI score of ≥ 2 , had the longest distance to the hospital, and in the period after CPP introduction.

3.1. Association between travel distance to health services and time intervals

No associations were observed between the patient's travel distance to the GP and the patient interval or the primary care interval for all cancer types combined (Table 3, Fig. 1a). However, stratified analysis showed that after 2010, longer distance to the GP was statistically significant associated with decreasing patient interval (β -0.330, p-value: < 0.001) (Table 3) and this association was statistically different in the two periods (p-value: < 0.001). No association was observed between the patient's travel distance to the hospital of diagnosis and the primary care interval. There was an association between distance to the hospital of diagnosis and the diagnostic interval (β 0.09, p-value: < 0.001) (Table 4, Fig. 1b). This indicates that longer travel distance increased the diagnostic interval, corresponding to an increase of approximately 6 days in the diagnostic interval when comparing a travel distance of 0 and 80 km. Further analyses showed that this association was strongest in the period before CPP implementation (< 2010) (β 0.18, p-value: < 0.001) compared to the period after CPP implementation (≥ 2010) (β 0.06, p-value: 0.049) (Table 4, Fig. 2). The association was statistically significantly different in the two periods (p-value: 0.014).

3.2. Association between travel distance to health services and time intervals according to diagnostic difficulty

After stratifying the analyses according to diagnostic difficulty, longer travel distance to the GP indicated shorter patient interval and

Table 2

Median and interquartile range (IQR) according to socio-demography, travel distance to the GP and hospital of diagnosis, diagnostic difficulty groups, time period before or after CPP for the patient interval, primary care interval, and diagnostic interval.

	Patient interval (n: 13,921 [*])			Primary care interval (n: 17,789 [*])			Diagnostic interval (n: 20,195 [*])		
	Median	(IQR)	P-value ^{**}	Median	(IQR)	P-value ^{**}	Median	(IQR)	P-value ^{**}
Total	9	(0-42)		1	(0-17)		34	(15-78)	
Age group, years			< 0.001			< 0.001			< 0.001
18-49	13	(1-61)		0	(0-10)		31	(14-71)	
50-59	14	(1-56)		0	(0-15)		31	(14-60)	
60-69	10	(0-47)		2	(0-17)		35	(16-79)	
70-79	7	(0-32)		3	(0-21)		36	(16-83)	
≥ 80	5	(0-30)		2	(0-20)		36	(15-90)	
Sex			0.312			< 0.001			< 0.001
Female	8	(0-42)		0	(0-13)		31	(14-69)	
Male	9	(0-42)		4	(0-21)		37	(17-78)	
Education			< 0.001			< 0.001			0.640
Low	7	(0-35)		2	(0-19)		35	(15-79)	
Middle	9	(0-43)		1	(0-17)		34	(15-77)	
High	13	(0-54)		0	(0-14)		34	(15-81)	
CCI ^{***}			< 0.001			0.001			< 0.001
0	10	(0-45)		1	(0-16)		32	(15-79)	
1-2	7	(0-35)		2	(0-18)		37	(15-77)	
> 2	7	(0-31)		2	(0-20)		43	(15-81)	
Distance to GP			0.930			0.284			0.568
0-2 km	8	(30.5)		1	(0-17)		35	(15-80)	
> 2-5 km	9	(31.1)		1	(0-16)		34	(15-77)	
> 5-10 km	10	(31.2)		2	(0-18)		35	(15-78)	
> 10 km	7	(27.9)		2	(0-19)		34	(15-77)	
Distance to hospital of diagnosis			0.384			0.215			0.006
0-10 km	10	(0-42)		1	(0-17)		34	(15-78)	
> 10-25 km	8	(0-42)		3	(0-20)		35	(15-81)	
> 25-50 km	8	(0-38)		1	(0-15)		31	(14-73)	
> 50 km	10	(0-45)		1	(0-17)		40	(18-86)	
Diagnostic difficulty level			< 0.001			< 0.001			< 0.001
Easy	8	(0-46)		0	(0-4)		27	(13-56)	
Intermediate	9	(0-46)		6	(0-22)		42	(19-99)	
Hard	8	(0-31)		7	(0-27)		36	(16-81)	
Cancer Patient Pathways (CPP)			< 0.001			0.046			< 0.001
Before (< 2010)	7	(0-31)		2	(0-18)		38	(18-84)	
After (≥ 2010)	12	(0-49)		1	(0-16)		31	(14-75)	

* Total number of responses.

** P-value, Wilcoxon rank-sum test for sex, Kruskal-Wallis test for diagnostic difficulty level. For the remaining variables: NP test for linear trend of the continuous interval variable.

*** Charlson's Comorbidity Index score.

Table 3

The association between distance to the GP and the patient interval and primary care interval.

Distance to GP for [*] :	Patient interval		Primary care interval	
	β ^{**}	P-value	β ^{**}	P-value
All patients	0.03	0.458	-0.04	0.077
Diagnostic difficulty level:				
Easy	0.02	0.939	***	***
Intermediate	-0.09	0.020	-0.06	< 0.01
Hard	-0.03	0.426	-0.05	0.052
Time period				
< 2010	-0.02	0.352	***	***
≥ 2010	-0.33	< 0.01	***	***

* Travel distance from the patient to the GP.

** Increase in days per increased km to the GP adjusted for sex, age, education, CCI and cohort.

*** Due to low variation in the primary care interval for these groups, this model did not converge and is omitted.

shorter primary care interval among patients categorised as 'intermediate to diagnose' (Table 3, Fig. 3). Stratifying the association between the distance to the hospital and the diagnostic interval according to diagnostic difficulty showed that the increasing diagnostic interval

with increasing distance (β 0.11, p-value: 0.014) was primarily caused by patients with 'hard to diagnose' cancer types (Table 4, Fig. 4), which indicates an increase in the diagnostic interval of almost 9 days when comparing a travel distance of 0 and 80 km.

4. Discussion

4.1. Main findings

In this population-based cohort study on travel distances and time intervals, we found that longer travel distance between the residence of the patient and the diagnosing hospital was associated with longer diagnostic intervals. This association was primarily driven by cancer patients diagnosed with cancer types that were hard to diagnose. Furthermore, this association was strongest in the period before the implementation of CPPs (< 2010). Longer travel distance to the GP for patients with 'intermediate to diagnose' cancer types was associated with shorter patient interval and shorter primary care interval and after 2010 longer travel distance to the GP was associated with shorter patient interval.

4.2. Strengths and limitations

This study included more than 20,000 cancer patients in the

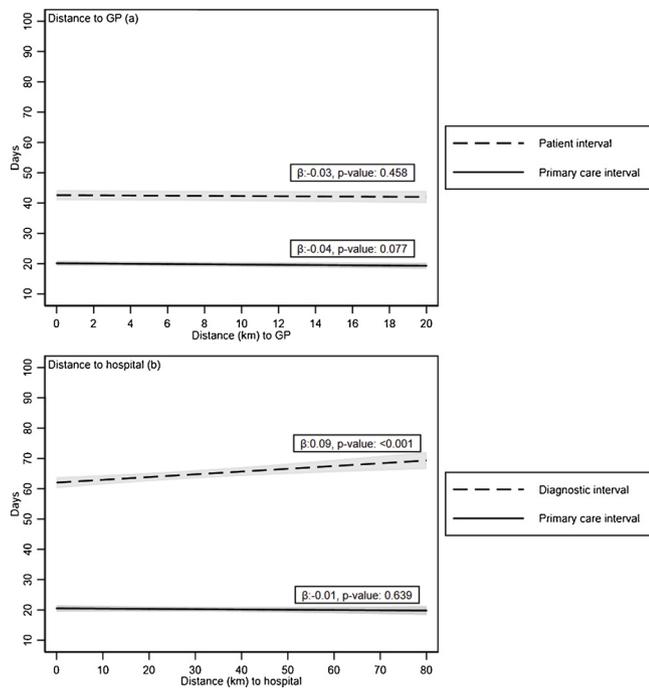


Fig. 1. Travel distance to the GP (a) and the association with the patient interval and the primary care interval. Travel distance to the hospital (b) and the association with the primary care interval and the diagnostic interval. Adjusted for sex, age, education, CCI, and sub-cohort. The beta coefficients and p-values for the adjusted associations are shown in each graph.

Table 4

The association between distance to the hospital of diagnosis and the primary care interval and the diagnostic interval.

Distance to hospital for *	Primary care interval		Diagnostic interval	
	β **	P-value	β **	P-value
All patients	0.01	0.639	0.09	< 0.01
Diagnostic difficulty level:				
Easy	-0.02	0.172	0.07	0.825
Intermediate	-0.02	0.424	0.09	0.074
Hard	-0.05	0.078	0.11	0.014
Time period				
< 2010	-0.02	0.179	0.18	< 0.01
≥ 2010	-0.01	0.601	0.06	0.049

* Travel distance from the patient to the hospital of diagnosis.
 ** Increase in days per increased km to the hospital adjusted for sex, age, education, CCI and cohort.

analyses and made it one of the largest in the literature. Therefore, this study achieved high statistical precision. Although the applied methods were adapted from the Aarhus statement [42], risk of information bias (especially recall bias) can be a concern for the intervals in the cancer trajectory [31,43]. However, differential recall of milestone dates are not likely to be related to travel distance and may be of minor importance in this study. Selection bias may have affected the findings as patient groups with low socio-economic position and morbidity are less likely to participate in surveys [31]. Still, the Danish registers included all cancer patients diagnosed in the study period, which ensured that no patients were excluded a priori. Furthermore, this collection of detailed patient- and GP-reported measures of milestone dates represents one of the largest samples in its field.

We had access to data from valid and complete Danish registries [32,33,35]. We obtained the home address of each patient on the date of diagnosis, and this enabled us to calculate the precise travel distance

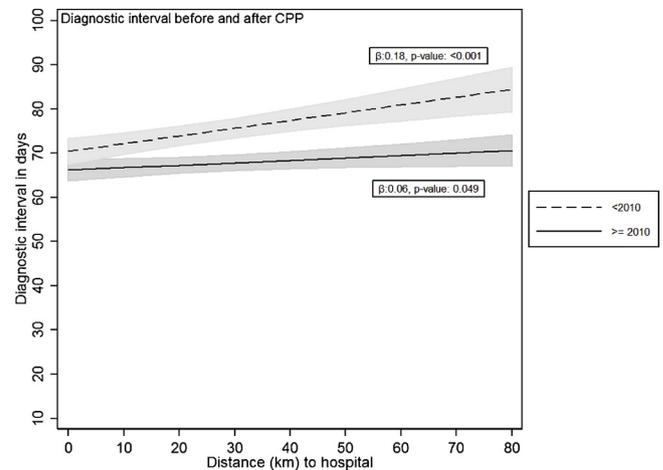


Fig. 2. Travel distance to the hospital and the association with the diagnostic interval stratified before (< 2010) and after (≥ 2010) the CPP. The dashed line represents the period before the CPP, and the solid line represents the period after the CPP. Adjusted for sex, age, education, CCI, and sub-cohort. The beta coefficients and p-values for the adjusted association are shown for each line.

from each patient’s residence to the GP and the diagnosing hospital. Register data was also used to assess potential confounders, such as SEP and comorbidity. Residual confounding cannot be ruled out as the association between travel distance and cancer outcomes are complex [23]. Thus, information on e.g. public transportation and delays due to traffic in urban areas or e.g. complicated travelling due to flights or ferries could have provided further insights into the association but these information’s were not available. This would however, probably affect ‘travel time’ more than the actual distance in km, however, in Denmark few people live in islands or in very remote areas.

Using linear regression to analyse the findings entails an assumption on linearity between distance and intervals whereas e.g. cubic spline analysis allow for non-linear associations. Cubic splines analysis were explored as well and the results lead to identical conclusions. Cubic splines does not provide one measure of association i.e. the beta, thus, it was chosen to present the linear regression.

It was not possible to calculate the distances for patients who were not listed with a specific GP or could not be identified with a diagnosing hospital in the DNPR [32]. However, this constitutes a small proportion of the population and is not likely to have affected the results.

Finally, this study is restricted to symptomatic patients as the included intervals only can be assessed for this group. Studies are warranted for the association between travel distance and the diagnostic process for asymptomatic patients, e.g. patients diagnosed through screening.

4.3. Interpretations of findings

Only few studies have previously studied travel distance to health services and associations with time intervals in the diagnostic process [17,23,24]. To our knowledge, no previous studies have explored the intervals in the pre-diagnostic phases, i.e. the primary care interval and the diagnostic interval.

The results from the sparse literature are generally inconclusive with several possible explanations. First, travel distance to cancer facilities may affect time intervals differently as the intervals require action by different actors [42]. For the patient interval, the primary actor is the patient and relatives, where travel distance may hamper health care seeking, as found in one study [17], if longer distance to health care poses a barrier for the patient. Contrarily, the primary care interval and the diagnostic interval are largely dependent on action from health professionals, who could perceive barriers differently than the patient. Second, travel distance to different health care providers

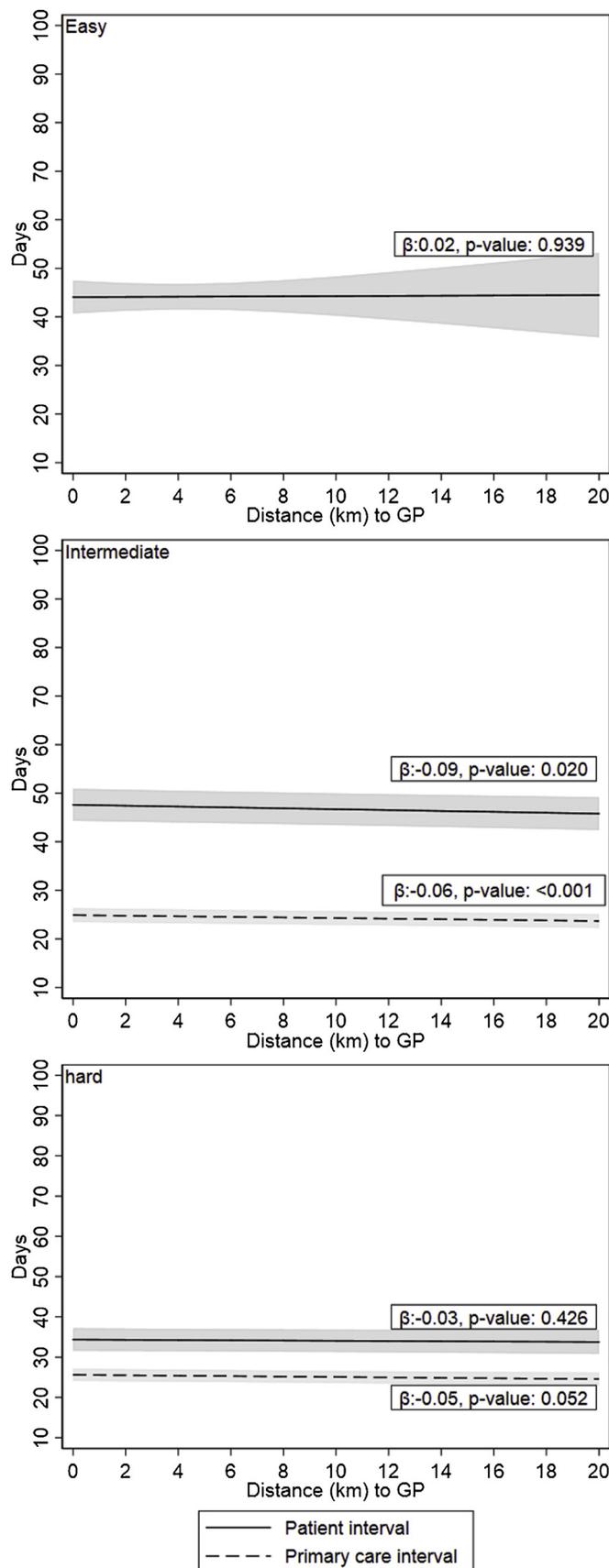


Fig. 3. Adjusted association between travel distance from the patient to the GP and the patient interval and the primary care interval* stratified according to diagnostic difficulty level. The solid line represents the patient interval, and the dashed line represents the primary care interval. Adjusted for sex, age, education, CCI, and sub-cohort. The beta coefficients and p-values for the adjusted associations are shown in each graph.

*Due to low variation in the primary care interval for the ‘easy to diagnose’ cancer types, this model did not converge and is omitted.

(e.g. primary or hospital care) may affect intervals differently. This is supported by the present study, which indicates that the studied intervals were affected differently by different distances, which was also reported in another study [23].

Health professionals is often guided by patient’s symptoms in the diagnostic pathway, as the cancer type is not known before a diagnosis is confirmed. Thus, an important finding in this study is that the association between travel distance and time intervals was modified by the diagnostic difficulty of the cancer, which is based on the underlying symptom. This may also explain the mixed findings reported for different cancer types [24]. It could be hypothesised that patients presenting with alarm symptoms (i.e. ‘easy to suspect’ cancer types) would not be affected by prolonged travel distance as both patients and health professionals more often would have indications of serious illness and rapidly present, refer, or investigate, whereas patients presenting with vague or unspecific symptoms might be more affected by distance. We saw longer diagnostic intervals in patients with longer distance who presented with ‘hard to suspect’ cancer types. As longer travel distance was not associated with the primary care interval in this group, this result could indicate that the delay was caused by barriers relating to the transition between sectors or to the diagnostic process at the hospital.

This study demonstrated that the longer diagnostic interval associated with travel distance became less pronounced in the period after the implementation of CPPs. The focus on cancer control in Denmark and many European countries has led to several health care changes during the recent two decades, including the introduction of CPPs [29], cancer plans in 2000, 2005, and 2010 [44–46], organised screening programmes for breast cancer (in 2008/09) [47] and colorectal cancer (in 2014/2015) [48], and cancer awareness campaigns. Although this study does not provide causal evidence that implementing standardised CPPs reduces the geographical inequality in the time to diagnosis, the study does indicate less variation in the diagnostic intervals across travel distance to health services in a period after introducing health care reforms aiming to improve cancer control.

The association between travel distance and time intervals in the diagnostic process is not straightforward [15,23]. It cannot be ruled out that the measure of distance also incorporates a component of e.g. cultural differences. Thus, the perception of distance may differ between countries or between patients living more remotely than patients living in urban areas. Only few and older qualitative studies exist [21,22]. More research from various methodological disciplines are needed to explore different perceptions of distance in patients and how these may affect their help-seeking behavior. Further, as the association between diagnostic pathways and prognosis is not always clear and comparable across cancer types, the importance of studies on prognosis and the impact of travel distance for specific cancer types are warranted as well.

5. Conclusion

This cohort study found that the travel distance from the patient’s residence to the GP was not associated with the time intervals in diagnostic journey in the main analyses. Travel distance to the hospital was associated with an increase in the length of the diagnostic interval, with increasing strength for increasing diagnostic difficulty. The

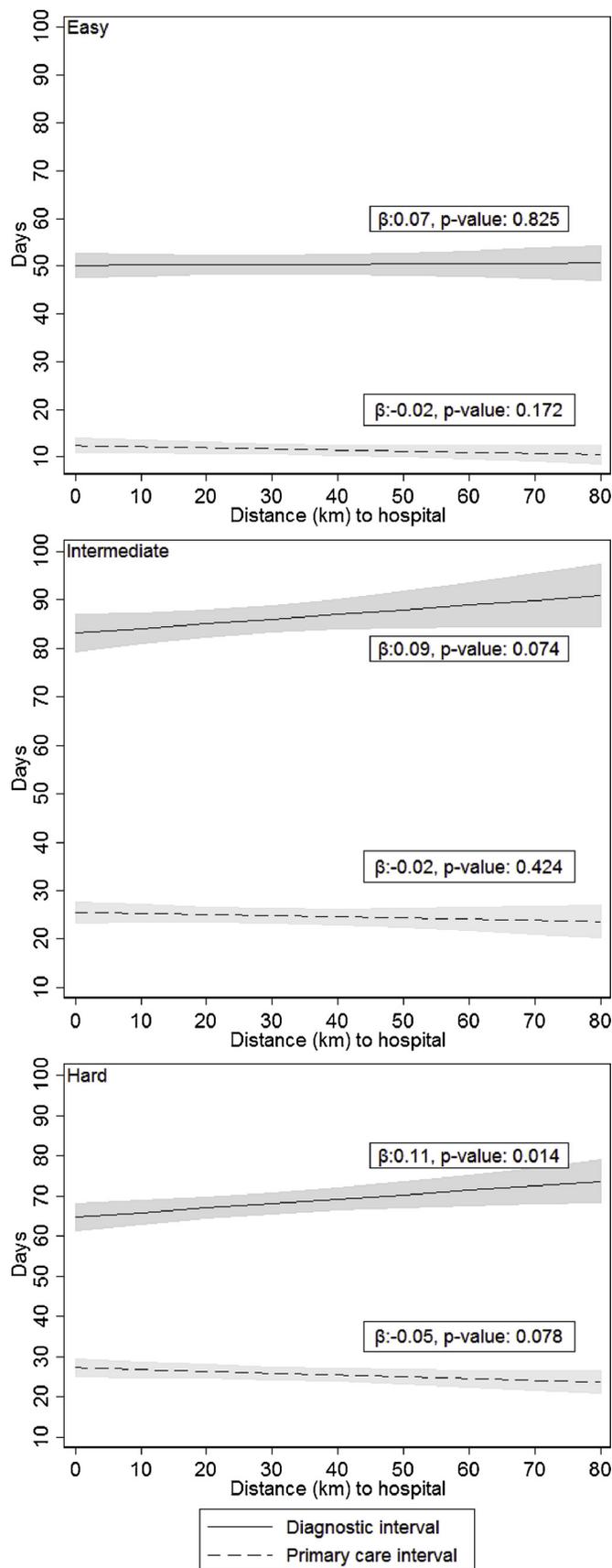


Fig. 4. Adjusted association between travel distance from the patient to the hospital of diagnosis and the primary care interval and the diagnostic interval stratified according to the diagnostic difficulty level. The solid line represents the diagnostic interval, and the dashed line represents the primary care interval. Adjusted for sex, age, education, CCI, and sub-cohort. The beta coefficients and p-values for the adjusted associations are shown in each graph.

association was reduced over time concurrently with structural changes in the health care system.

Authors’ contribution

LFV, HM, and PV conceived the idea and contributed with input and critical revision of the statistical analyses and the contents of the paper. LFJ was primarily responsible for drafting the manuscript and for the statistical analyses performed on the platform of Statistics Denmark. All authors read and approved the final version of the manuscript, and LFV had the final responsibility to submit the paper.

Declaration of interests

The authors declare that there are no conflicts of interests.

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References

- [1] M.L. Topping, M. Frydenberg, W. Hamilton, R.P. Hansen, M.D. Lautrup, P. Vedsted, Diagnostic interval and mortality in colorectal cancer: U-shaped association demonstrated for three different datasets, *J. Clin. Epidemiol.* 65 (2012) 669–678.
- [2] M.L. Topping, M. Frydenberg, R.P. Hansen, F. Olesen, P. Vedsted, Evidence of increasing mortality with longer diagnostic intervals for five common cancers: a cohort study in primary care, *Eur. J. Cancer* 49 (2013) 2187–2198.
- [3] R.D. Neal, V.L. Allgar, Sociodemographic factors and delays in the diagnosis of six cancers: analysis of data from the "National Survey of NHS Patients: Cancer", *Br. J. Cancer* 92 (2005) 1971–1975.
- [4] Ministry of Health and Prevention, Health Care in Denmark, Ministry of Health and Prevention, Copenhagen, 2008.
- [5] A. Oliver, E. Mossialos, Equity of access to health care: outlining the foundations for action, *J. Epidemiol. Community Health* 58 (2004) 655–658.
- [6] M. Luchtenborg, S.P. Riaz, V.H. Coupland, E. Lim, E. Jakobsen, M. Krasnik, et al., High procedure volume is strongly associated with improved survival after lung cancer surgery, *J. Clin. Oncol.* 31 (2013) 3141–3146.
- [7] S. Brown, A centralized system to access acute healthcare services: the pros and cons, *Healthc. Manag. Forum* 18 (2005) 34–37.
- [8] K.B. Stitzenberg, E.R. Sigurdson, B.L. Egleston, R.B. Starkey, N.J. Meropol, Centralization of cancer surgery: implications for patient access to optimal care, *J. Clin. Oncol.* 27 (2009) 4671–4678.
- [9] A.P. Jones, R. Haynes, V. Sauerzapf, S.M. Crawford, H. Zhao, D. Forman, Travel time to hospital and treatment for breast, colon, rectum, lung, ovary and prostate cancer, *Eur. J. Cancer* 44 (2008) 992–999.
- [10] A.P. Jones, R. Haynes, V. Sauerzapf, S.M. Crawford, H. Zhao, D. Forman, Travel times to health care and survival from cancers in Northern England, *Eur. J. Cancer* 44 (2008) 269–274.
- [11] N.N. Massarweh, Y.J. Chiang, Y. Xing, G.J. Chang, A.B. Haynes, Y.N. You, et al., Association between travel distance and metastatic disease at diagnosis among patients with colon cancer, *J. Clin. Oncol.* 32 (2014) 942–948.
- [12] N.C. Campbell, A.M. Elliott, L. Sharp, L.D. Ritchie, J. Cassidy, J. Little, Rural and urban differences in stage at diagnosis of colorectal and lung cancers, *Br. J. Cancer* 84 (2001) 910–914.
- [13] R. Haynes, J. Pearce, R. Barnett, Cancer survival in New Zealand: ethnic, social and geographical inequalities, *Soc. Sci. Med.* 67 (2008) 928–937.
- [14] K.A. Henry, F.P. Boscoe, C.J. Johnson, D.W. Goldberg, R. Sherman, M. Cockburn, Breast cancer stage at diagnosis: is travel time important? *J. Commun. Health* 36 (2011) 933–942.
- [15] P. Murage, P. Murchie, M. Bachmann, M. Crawford, A. Jones, Impact of travel time and rurality on presentation and outcomes of symptomatic colorectal cancer: a cross-sectional cohort study in primary care, *Br. J. Gen. Pract.* 67 (2017) e460–e466, <https://doi.org/10.3399/bjgp17X691349>.
- [16] D. Weller, P. Vedsted, G. Rubin, F.M. Walter, J. Emery, S. Scott, et al., The Aarhus statement: improving design and reporting of studies on early cancer diagnosis, *Br.*

- J. Cancer 106 (2012) 1262–1267.
- [17] F. Ouasmani, Z. Hanchi, B. Haddou Rahou, R. Bekkali, S. Ahid, A. Mesfioui, Determinants of patient delay in seeking diagnosis and treatment among moroccan women with cervical cancer, *Obstet. Gynecol. Int.* 2016 (2016) 4840762.
- [18] B.T. Chan, P.C. Austin, Patient, physician, and community factors affecting referrals to specialists in Ontario, Canada: a population-based, multi-level modelling approach, *Med. Care* 41 (2003) 500–511.
- [19] R.P. Hansen, P. Vedsted, I. Sokolowski, J. Sondergaard, F. Olesen, Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients, *BMC Health Serv. Res.* 11 (2011) 284-6963-11-284.
- [20] V.L. Allgar, R.D. Neal, General practitioners' management of cancer in England: secondary analysis of data from the National Survey of NHS Patients-Cancer, *Eur. J. Cancer Care (Engl)* 14 (2005) 409–416.
- [21] F. Brundisini, M. Giacomini, D. DeJean, M. Vanstone, S. Winsor, A. Smith, Chronic disease patients' experiences with accessing health care in rural and remote areas: a systematic review and qualitative meta-synthesis, *Ont. Health Technol. Assess. Ser.* 13 (2013) 1–33.
- [22] N.S. Bain, N.C. Campbell, Treating patients with colorectal cancer in rural and urban areas: a qualitative study of the patients' perspective, *Fam. Pract.* 17 (2000) 475–479.
- [23] M. Turner, S. Fielding, Y. Ong, C. Dibben, Z. Feng, D.H. Brewster, et al., A cancer geography paradox? Poorer cancer outcomes with longer travelling times to healthcare facilities despite prompter diagnosis and treatment: a data-linkage study, *Br. J. Cancer* 117 (2017) 439–449.
- [24] N.C. Campbell, A.M. Elliott, L. Sharp, L.D. Ritchie, J. Cassidy, J. Little, Impact of deprivation and rural residence on treatment of colorectal and lung cancer, *Br. J. Cancer* 87 (2002) 585–590.
- [25] G. Lyrtzopoulos, J. Wardle, G. Rubin, Rethinking diagnostic delay in cancer: how difficult is the diagnosis? *BMJ* 349 (2014) g7400.
- [26] G. Lyrtzopoulos, R.D. Neal, J.M. Barbiere, G.P. Rubin, G.A. Abel, Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer patient Experience Survey in England, *Lancet Oncol.* 13 (2012) 353–365.
- [27] M.M. Koo, W. Hamilton, F.M. Walter, G.P. Rubin, G. Lyrtzopoulos, Symptom signatures and diagnostic timeliness in cancer patients: a review of current evidence, *Neoplasia* 20 (2018) 165–174.
- [28] K.M. Pedersen, J.S. Andersen, J. Sondergaard, General practice and primary health care in Denmark, *J. Am. Board Fam. Med.* 25 (Suppl. 1) (2012) S34–8.
- [29] F. Olesen, R.P. Hansen, P. Vedsted, Delay in diagnosis: the experience in Denmark, *Br. J. Cancer* 101 (Suppl. 2) (2009) S5–8.
- [30] H. Jensen, M.L. Topping, F. Olesen, J. Overgaard, M. Fenger-Gron, P. Vedsted, Diagnostic intervals before and after implementation of cancer patient pathways - a GP survey and registry based comparison of three cohorts of cancer patients, *BMC Cancer* 15 (2015) 308-015-1317-7.
- [31] H. Jensen, M.L. Topping, M.B. Larsen, P. Vedsted, Existing data sources for clinical epidemiology: Danish cancer in primary care cohort, *Clin. Epidemiol.* 6 (2014) 237–246.
- [32] E. Lyng, J.L. Sandegaard, M. Rebolj, The Danish national patient register, *Scand. J. Public Health* 39 (2011) 30–33.
- [33] J.S. Andersen, F. Olivarius Nde, A. Krasnik, The Danish national health service register, *Scand. J. Public Health* 39 (2011) 34–37.
- [34] C.B. Pedersen, The Danish civil registration system, *Scand. J. Public Health* 39 (2011) 22–25.
- [35] M.L. Gjerstorff, The Danish Cancer registry, *Scand. J. Public Health* 39 (2011) 42–45.
- [36] A. Falborg, H. Jensen, P. Vedsted, U. Menon, D. Weller, ICBP Module 1 Working Group, Does Data From Questionnaires and Cancer Registries Agree on Routes and Time Intervals to Diagnosis? *CaPri Abstract Book*, 2017 2017.
- [37] ESRI, *ArcGIS Network Analyst*, (2014) Available at:<http://www.esri.com/software/arcgis/extensions/networkanalyst> Accessed 02 February 2019.
- [38] UNESCO, *ISCED: International Standard Classification of Education*, (2014) Available at:<http://www.uis.unesco.org/Education/Pages/international-standard-classification-of-education.aspx> Accessed 02 February 2019.
- [39] J. Cuzick, A Wilcoxon-type test for trend, *Stat. Med.* 4 (1985) 87–90.
- [40] D. Weller, P. Vedsted, C. Anandan, A. Zalounina, E.O. Fourkala, R. Desai, et al., An investigation of routes to cancer diagnosis in 10 international jurisdictions, as part of the international cancer benchmarking partnership: survey development and implementation, *BMJ Open* 6 (2016) e009641-2015-009641.
- [41] European Commission, *Data Protection*, (2018) Available at:https://ec.europa.eu/info/law/law-topic/data-protection_en Accessed 17 October 2018.
- [42] D. Weller, P. Vedsted, G. Rubin, F.M. Walter, J. Emery, S. Scott, et al., The Aarhus statement: improving design and reporting of studies on early cancer diagnosis, *Br. J. Cancer* 106 (2012) 1262–1267.
- [43] R.S. Andersen, P. Vedsted, F. Olesen, F. Bro, J. Sondergaard, Patient delay in cancer studies: a discussion of methods and measures, *BMC Health Serv. Res.* 9 (2009) 189-6963-9-189.
- [44] National Board of Health, *National Cancer Plan II - Denmark: National Board of Health Recommendations for Improving Cancer Healthcare Services*. Version: 1, 0 ed. Sundhedsstyrelsen, Copenhagen, 2005.
- [45] National Board of Health, *Styrket indsats på kræftområdet – et sundhedsfagligt oplæg 2010* [English: A stronger effort of cancer], National Board of Health, Copenhagen, 2008.
- [46] National Board of Health, *National kræftplan: status og forslag til initiativer i relation til kræftbehandlingen*. Kbh. Sundhedsstyrelsen, 2000.
- [47] I. Vejborg, E. Mikkelsen, J.P. Garne, M. Bak, A. Lernevall, N.B. Mogensen, et al., Mammography screening in Denmark, *Dan. Med. Bull.* 58 (2011) C4287.
- [48] The Danish Health Authority, *Tarmkræftscreening [Colorectal Cancer Screening]*, (2016) 2018.