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Patient characteristics and cancer prevalence in the Danish cancer patient pathway for patients with serious non-specific symptoms and signs of cancer—A nationwide, population-based cohort study

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ABSTRACT

Background: A new cancer patient pathway for patients presenting with non-specific signs and symptoms (NSSC-CPP) was implemented nationally in Denmark in 2012. This study aims to describe, on a national level, the characteristics of patients referred to the Danish NSSC-CPP, and to estimate the prevalence and distribution of cancers and other diagnosis in this population.
Methods: A population-based cohort study using the Danish national registries, including all patients who completed a diagnostic course through the NSSC-CPP between 2012 and 2015. Cancer prevalence is presented as the percentage of included patients who were diagnosed with cancer after completing a NSSC-CPP diagnostic course. Associations between patient characteristics and cancer diagnosis were estimated in a multivariate logistic regression model.
Results: The mean age of the 23,934 patients included in the analysis was 64.6 years and 47% where male. In total, 11% of all patients received a cancer diagnosis after completing a diagnostic course in the NSSC-CPP; the most common types were breast cancer (18%) hematopoietic and lymphoid tissue cancer (15%), and malignant melanoma (12%). The most common non-cancer diagnosis was non-specific symptoms/observation (54%). Fifty-five patients were diagnosed with cancer within six months following a non-cancer diagnosis in the NSSC-CPP.
Conclusions: The prevalence of cancer in the NSSC-CPP was 11%. The most common cancer diagnosis was breast cancer, hematopoietic and lymphoid cancer and malignant melanoma. A small proportion of patients receiving a non-cancer diagnosis in the NSSC-CPP were diagnosed with cancer in the six months following their NSSC-CPP course.

1. Introduction

Several countries including Denmark have implemented urgent referral Cancer Patient Pathways (CPPs) to ensure timely diagnosis of cancer [1–4]. In the UK, the two-week referral (2WW) system was introduced in 2000 [5–7], while CPPs were introduced in 2008 in Denmark [3,8]. The CPPs describe the patient's pathway from clinical suspicion through to diagnostic procedures and treatment [3]. Both UK and Danish studies have shown that implementation of urgent referral pathways has reduced the duration of the diagnostic interval from the patient's first presentation of symptoms in the healthcare system until diagnosis [8–10]. A shorter diagnostic interval may contribute to a more favourable stage distribution at diagnosis and better treatment options, which ultimately could have a positive impact on cancer mortality [11,12].

The primary focus of both the Danish and UK pathways are alarm symptoms supporting a clinical suspicion of a specific cancer [3,4]. However, studies have shown that only half of patients later diagnosed with cancer initially present with alarm symptoms [10,13,14]. Moreover, only approximately 40% of all cancer patients seem to have benefitted from the implementation of CPPs [8,10], and cancer patients not diagnosed through a CPP have been shown to have longer diagnostic intervals than patients diagnosed through a CPP [8]. Thus, the implementation of CPPs may have disadvantaged the large group of patients who present with symptoms not classified as typical alarm symptoms of cancer [8].

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Consequently, a CPP for patients suspected of having cancer due to serious non-specific symptoms (NSSC-CPP) was implemented nationally in Denmark in 2012 [15,16]. The objective was to enhance timely diagnosis, decrease psychosocial distress, and ultimately improve prognosis and quality of life in patients suspected of having a cancer illness [3]. The pathway consists of a two-step approach with an initial assessment performed by the general practitioner (GP), who is often the first provider in the NSSC-CPP, and, if still relevant, a referral to a diagnostic unit at the hospital level [15,16]. The initial assessment consists of standard diagnostic investigations, including diagnostic imaging and blood and urine tests, and this phase should be completed within eight days [15,16]. A diagnostic unit is a medical unit with extensive facilities for medical investigation, including easy access to expertise in relevant specialties [15,16]. Each of the five Danish regions has at least one diagnostic unit, and approximately 15 units have been established [15]. At the time of referral to a diagnostic unit, patients are informed that they are undergoing diagnostic evaluations through a CPP due to suspicion of serious illness that could be cancer [16]. The most common symptoms seen at referral are weight loss, fatigue, pain, and nausea [15,17,18]. A clinical coordinator is included in the pathway to optimize logistics, and the overall aim is to diagnose or refute cancer or any serious illness within 22 days [15,16]. Cancer prevalence rates between 16% and 18% have been reported in studies investigating the NSSC-CPP, and haematological, lung, and colorectal cancer were the most common cancer types [15,17,18]. These results are from single center studies limiting the generalizability of the results [17,18]. Hence, more information is needed on the characteristics of the patients referred to the NSSC-CPP and the specific diagnosis after completed diagnostic evaluation. The aim of this study was therefore, on a national level, to describe the characteristics of patients referred to the Danish NSSC-CPP, and to estimate the prevalence and distribution of cancers and other diagnosis in this population.

2. Material and methods

2.1. Study design and participants

This is a national population-based cohort study including all patients who completed a diagnostic course through the NSSC-CPP between March 1, 2012 and December 31, 2015. Patients were identified through the National Patient Registry (NPR) with the code for referral to the NSSC-CPP [AFA01A]. A NSSC-CPP diagnostic course was defined by the code for initiation of diagnostic evaluations [AFA01B] registered at the first outpatient visit in a diagnostic unit and a code for completing diagnostic evaluations, either as a result of a clinical decision [AFA01X1] or patient decision [AFA01X2]. All patients with at least one complete NSSC-CPP course were included. Patients were excluded if the referral date was prior to 2012, if they did not start a NSSC-CPP course (e.g. no registered AFA01B code), or if they did not end a NSSC-CPP course (not registered with the codes AFA01X1 or AFA01X2). If a patient was registered with two or more NSSC-CPP courses within a 30 day timeframe, this was defined as one diagnostic course. See flowchart in Fig. 1.

2.2. Procedures

Data was collected from the national registries in Denmark. The Danish healthcare system is tax financed and offers free, unrestricted health care to the entire Danish population (5.5 million people). Utilization of healthcare services is registered using a unique civil registration number (CPR-number). The number is assigned to each Danish citizen at birth and to residents upon immigration and allows unambiguous individual-level linkage of all national administrative and healthcare registries [19].

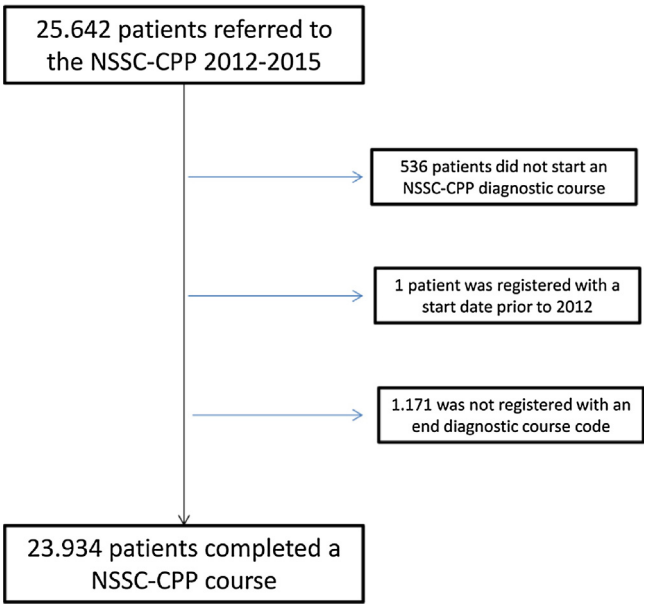

Fig. 1. Flowchart of inclusion and exclusion.

The following information was collected from the registries at Statistics Denmark: date of birth, sex, marital status, country of birth, socio-economic status, and education. The NPR contains information on all patients discharged form Danish non-psychiatric hospitals since 1977 and all outpatient- and emergency room visits since 1995 [20]. The following data was extracted from the NPR: hospital admissions during 2012–2015, including information on co-morbidity, referral, procedures performed during the NSSC-CPP course, geographical region of NSSC-CPP course, final diagnosis, and possible cancer diagnosis after completed NSSC-CPP course. Data on co-morbidity was extracted from 1995 to 2012 to account for comorbidity prior to referral to the NSSC-CPP. Diagnosis at the time of completed NSSC-CPP course was defined by the primary diagnosis given to the patient and all diagnoses are classified according to the International Classification of Diseases 10th Revision (ICD-10 codes). Patients registered with ICD-10 code C00-C97 as a primary diagnosis at the end of the NSSC-CPP course were classified as receiving a cancer diagnosis. Patients who received a cancer diagnosis in the week following completion of the diagnostic course were classified as receiving their diagnosis in the NSSC-CPP. Patients not diagnosed with cancer through the NSSC-CPP but who were subsequently diagnosed with a cancer illness in the six months following the NSSC-CPP course is defined as subsequent cancer. The NPR is considered to be precise and valid, and 95% of incident cancer diagnoses are displayed four months after diagnosis [20,21]. Comorbidities were scored according to the Charlson Comorbidity Index [22].

2.3. Statistical analysis

Categorical variables are described as counts (%), and continuous variables are described as means (SD) or medians with the 25th to 75th interquartile ranges (IQR). Cancer prevalence is presented as the percentage of included patients who were diagnosed with cancer after completing a NSSC-CPP course. Associations between different patient characteristics and cancer diagnosis in the NSSC-CPP were estimated in a multivariate logistic

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