

Predictive values of GPs' suspicion of serious disease:

a population-based follow-up study

Abstract

Background

Knowledge is sparse on the prevalence of suspicion of cancer and other serious diseases in general practice. Likewise, little is known about the possible implications of this suspicion on future healthcare use and diagnoses.

Aim

To study the prevalence of GPs' suspicions of cancer or other serious diseases and analyse how this suspicion predicted the patients' healthcare use and diagnoses of serious disease.

Design and setting

Prospective population-based cohort study of 4518 patients consulting 404 GPs in a mix of urban, semi-urban and rural practices in Central Denmark Region during 2008–2009.

Method

The GPs registered consultations in 1 work day, including information on their suspicion of the presence of cancer or another serious disease. The patients were followed up for use of healthcare services and new diagnoses through the use of national registers.

Results

Prevalence of suspicion was 5.7%. Suspicion was associated with an increase in referrals (prevalence ratio [PR] = 2.56, 95% confidence interval [CI] = 2.22 to 2.96), especially for diagnostic imaging (PR = 3.95, 95% CI = 2.80 to 5.57), increased risk of a new diagnosis of cancer or another serious disease within 2 months (hazard ratio [HR] = 2.98, 95% CI = 1.93 to 4.62) — especially for cancer (HR = 7.55, 95% CI = 2.66 to 21.39) — and increased use of general practice (relative risk [RR] = 1.14, 95% CI = 1.06 to 1.24) and hospital visits (RR = 1.90, 95% CI = 1.62 to 2.23). The positive predictive value of a GP suspicion was 9.8% (95% CI = 6.4 to 14.1) for cancer or another serious disease within 2 months.

Conclusion

A GP suspicion of serious disease warrants further investigation, and the organisation of the healthcare system should ensure direct access from the primary sector to specialised tests.

Keywords

Denmark; diagnosis; general practice; neoplasm; referral and consultation.

INTRODUCTION

General practice forms the first line of the healthcare system.¹ When patients present with symptoms and signs in general practice, the positive predictive values (PPVs) of serious disease are low (often <5%), whereas the frequency of 'low-risk-but-not-no-risk' symptoms and signs is high.^{2–7} This fundamental conflict constitutes a major clinical challenge for GPs and for the organisation of the entire healthcare system.

In a Norwegian study, warning signs of cancer were identified in 12.4% of GP consultations and, among these, the GPs suspected 24% to have cancer.^{8,9} This indicates that GPs do not always use specific 'alarm' symptoms to identify serious disease and start a diagnostic process.^{9,10} A Danish study found that approximately half of patients with cancer (depending on cancer type) did not present with alarm symptoms.¹¹ This important group of patients was not investigated in, for example, the Norwegian studies; knowledge is still lacking, therefore, about how often GPs suspect serious disease among all patients. Nylenna found that a suspicion of cancer prompted GPs to initiate further investigation in 4.2% of patients in general practice of whom 7.8% were later diagnosed with cancer.^{12,13}

However, Nylenna's study, and similar studies, may be influenced by the Hawthorne effect, and GPs' awareness of cancer could be influenced by the study

itself. How often GPs suspect cancer and serious disease in daily practice among all patients must be acknowledged; and this knowledge should not be confounded by the awareness that researchers are looking for specific diseases. Further, it is essential to know how GPs act when a suspicion of serious disease is raised and how such suspicion may predict serious diagnoses. This knowledge is crucial in order to optimise support for GPs when patients are suspected of having a serious disease.

The aims of this study were to:

- describe how often GPs in Denmark suspect cancer or other serious disease after a consultation;
- characterise the patients in whom suspicion was raised;
- describe how the GPs acted on their suspicion; and
- analyse how a suspicion may influence the demand for healthcare services and predict a future diagnosis of serious disease.

METHOD

Study design

All 845 GPs serving approximately 1.2 million inhabitants in the Central Denmark Region were invited to participate in the KOS 2008 study, a survey on reasons for encounter and disease patterns in Danish general practice.¹⁴ During the 12-month period

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How this fits in

Patients eligible for a diagnostic fast track (for example for cancer) must have specific symptoms. However, only half of the patients who are later diagnosed with cancer initially present with 'alarm' symptoms in general practice. This study shows that GPs suspect cancer or another serious disease, on average, once per day. Such suspicion is associated with the need for referral to specialised testing, a hazard ratio of 7.6, and a positive predictive value of 2.3% of cancer within 2 months. Therefore, the healthcare system must support the diagnostic work-up on patients referred from general practice when serious disease is suspected as the PPV resembles that of alarm symptoms.

from December 2008 to December 2009, participating GPs were randomly assigned a work day on which they had to record all patient contacts. The GPs received payment for their participation (€32) and for each registered contact (€3).

Data

The registration form included a range of questions addressing the following themes:

- basic clinical information on the patient;
- chronic diseases;
- type of contact;
- reason for encounter;
- content of the contact;
- actions taken (referrals, clinic tests, and follow-up appointments); and
- the question: 'Are you left with the slightest suspicion of cancer or another serious disease (new)?'.

Reasons for encounter and diagnoses were written in text or stated by codes using the *International Classification of Primary Care* (ICPC-2).¹⁵ Diagnoses in text were coded subsequently by an experienced medical student, who was trained in ICPC coding. All codes were subsequently validated by one of the authors. Information on the number of chronic diseases was collected from the registration form and categorised as: 0, 1–2, or ≥ 3 .

Outcome

The unique personal identification number assigned to all Danish citizens at birth enabled linkage of information from various national health registries. The Danish

National Registry of Patients¹⁶ was used to register all new, serious, hospital-based diagnoses and use of hospital services for each patient during the 6 months following the index consultation. Diagnoses were coded using the tenth revision of the *International Classification of Diseases* (ICD-10).¹⁷ For each person only incident diagnoses were included, so that diagnoses registered between January 2000 and the index consultation were excluded.

Serious diseases other than cancer were defined by independently reviewing all new diagnoses (four-digit code, for example, A415) for the patients while blinded to the GP registrations. Disagreements were discussed and consensus reached. Non-melanoma skin cancers (DC44) were not included as they differ substantially regarding treatment and prognosis compared to other cancers. The full list of included serious diseases is available from the author. To test the possible effect on PPVs and hazard ratios (HRs) of adding less-serious diseases as outcomes, sensitivity analyses were performed including only definite serious diseases.

Hospital services included inpatient stays, outpatient visits, diagnostic imaging, and endoscopies (gastroscopy, colonoscopy, and sigmoidoscopy). Data on diagnostic imaging and endoscopic investigations performed by primary-care specialists, as well as use of general practice and practising specialists, were obtained from the Danish National Health Insurance Service Registry.¹⁸ Contacts to general practice were defined as face-to-face consultations, including home visits. Contacts to practising specialists included all contacts to practising specialists in dermatology, neurology, surgery, gynaecology, psychiatry, otorhinolaryngology, and internal medicine.

Data on sociodemographic variables from Statistics Denmark were included on marital status (married/cohabiting or living alone) and labour-market status (working, retired/receiving pension, or out of the workforce [unemployment, incapacity, or sickness]). Income was defined as the Organisation for Economic Cooperation and Development-adjusted household income for the year of the consultation, adjusted for number of persons in the household and divided into quartiles based on included patients.^{19,20}

Statistical analyses

Associations between patient characteristics and suspicion of serious disease were analysed using generalised linear models (GLMs) from the binomial family, with either identity link (for prevalence differences)

or logarithmic link (for prevalence ratios). Robust variance estimation accounting for clustering at GP level was performed. A similar GLM model was used to investigate associations between suspicion and actions taken during the consultation.

Cox proportional hazard models, with time to diagnosis as the outcome variable, were used to calculate the risk of being diagnosed with a new serious disease in the period from the index consultation until 2 months later (61 days) and 2–6 months later (62–183 days). Patients were censored at the date of diagnosis, at death, or 6 months after the consultation, whichever came first. The use of healthcare services was compared using a GLM, including adjustment for the use of each service in the year preceding the consultation (dichotomous). The outcome was dichotomised into consultation or no consultation. Use of GP was analysed both as a continuous and dichotomous variable to test for consistency of results.

Multivariate analyses were adjusted for age group (18–39 years, 40–54 years, 55–69 years, ≥ 70 years), sex, marital status, income, chronic diseases (0, 1–2, ≥ 3), and risk time. The Cox regression was adjusted for age as a continuous variable, with sex and chronic diseases coded as dichotomous variables (0, ≥ 1). All analyses were carried

out using the statistical software Stata (version 12.1).

RESULTS

A total of 404 of the 845 invited GPs participated. The proportion of female GPs among participating GPs was higher than in the Central Denmark Region [44.6% versus 38.9%, $P = 0.002$] and the proportion of GPs with >20 years experience was lower among participating GPs than in Central Denmark Region (20.1% versus 25.5%, $P = 0.007$).¹⁴

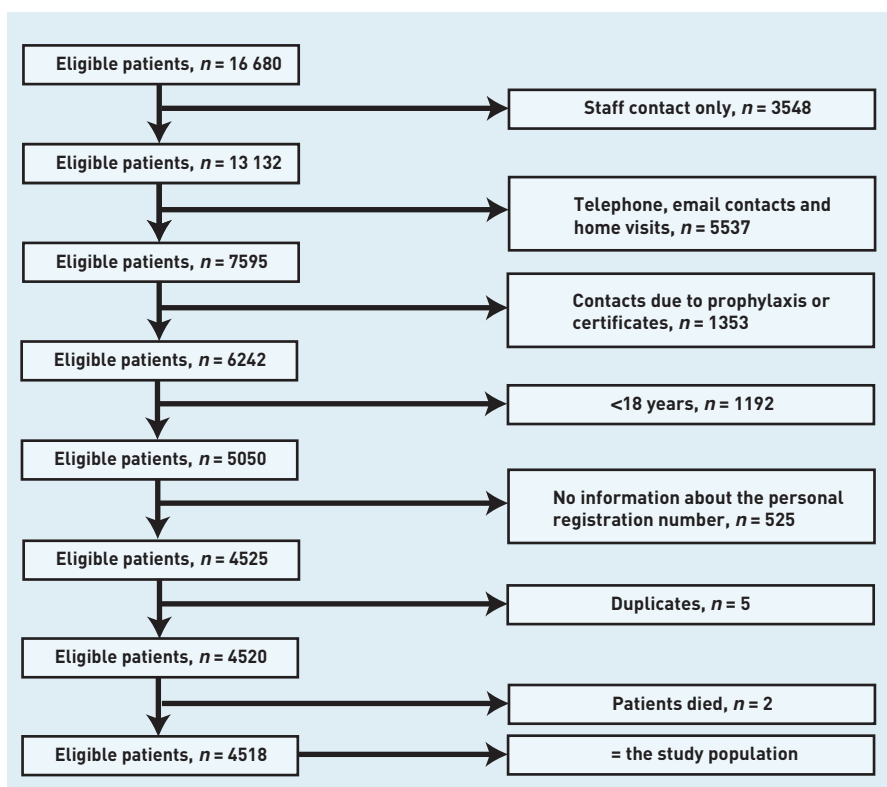
In total, 16680 contacts were registered (Figure 1); of these, 4518 patients had a face-to-face consultation with a GP, were aged ≥ 18 years and were registered with their complete information on a personal identification number. GPs suspected cancer or another serious disease after the consultation in 256 (5.7%, 95% confidence interval [CI] = 5.0 to 6.4) encounters. In 191 (4.2%) of the consultations, this information was missing. To preserve statistical power, the study included these as having no suspicion.

The prevalence of suspicion was highest among males, older patients, patients with chronic diseases, and retired individuals (Table 1). There was no association with patient income. The effect of age remained statistically significant when associated with suspicion in the multivariate analysis (Table 1). The prevalence of suspicion was highest among patients presenting symptoms from blood, blood-forming organs, digestive organs, and female genital organs (Table 1). The suspicion was lowest in patients presenting with psychological problems or symptoms from the musculoskeletal, endocrine, and cardiovascular systems.

The overall probability of being referred was 2.56 times higher in patients for whom serious disease was suspected, ranging from 1.45 for other referrals to 3.95 for diagnostic imaging (Table 2). Suspicion increased the probability of having a test conducted in the GP clinic and increased the likelihood of a follow-up appointment (Table 2).

The risk of a diagnosis of cancer or another serious disease was higher within the first 2 months after the index consultation for patients with a suspicion compared with those with no suspicion (adjusted HR = 2.98, 95% CI = 1.93 to 4.62) and remained increased during 2–6 months after the consultation (HR = 1.52, 95% CI = 0.92 to 2.53, $P = 0.103$) (Table 2). This pattern was the same when stratified into cancer and other serious diseases. The PPV of GPs' suspicion for later diagnosis of

Figure 1. Flow chart of patient inclusion.



serious disease or cancer was 9.8% [95% CI = 6.4 to 14.1] within the first 2 months after the index consultation (Table 3).

Of the 42 persons in whom the GP's suspicion was confirmed, 22 (52.4%, 95% CI = 37.7 to 66.6) had a reason for encounter clearly related to the subsequent diagnosis, for example, intermenstrual

bleeding and endometrial cancer (data not shown). Among the 279 patients with a later serious diagnosis, in whom the GP had not suspected serious disease, 62 (22.2%, 95% CI = 17.7 to 27.5) had a diagnosis related to their reason for encounter (data not shown).

Inclusion of only definite serious diseases in the analysis resulted in a PPV of 5.5%

Table 1. Patient characteristics and GPs' suspicions of serious disease after consultation

Characteristic		All contacts <i>n</i>	Prevalence of suspicion, ^a <i>n</i> (%)	Prevalence difference, % (95% CI)	Crude prevalence ratio (95% CI)	Adjusted ^b prevalence ratio (95% CI)
All		4518	256 (5.7)			
Age, years ^c	18–39	1367	38 (2.8)	Ref	1	1
	40–54	1157	48 (4.2)	1.4 (0.0 to 2.8)	1.49 (0.98 to 2.27)	1.50 (0.93 to 2.41)
	55–69	1153	90 (7.8)	5.0 (3.3 to 6.8)	2.81 (1.94 to 4.07)	2.73 (1.73 to 4.30)
	≥70	841	80 (9.5)	6.7 (4.6 to 8.9)	3.42 (2.35 to 4.99)	3.07 (1.98 to 4.76)
Sex	Female	2802	141 (5.0)	Ref	1	1
	Male	1716	115 (6.7)	1.7 (0.2 to 3.1)	1.33 (1.05 to 1.69)	1.24 (0.98 to 1.56)
Marital status	Married/cohabiting	3007	154 (5.1)	Ref	1	1
	Living alone	1499	101 (6.7)	1.6 (0.1 to 3.1)	1.32 (1.03 to 1.68)	1.30 (0.98 to 1.72)
Labour-market status	Working	2643	105 (4.0)	Ref	1	1
	Retired/receiving pension	1600	136 (8.5)	4.5 (3.0 to 6.1)	2.14 (1.67 to 2.74)	1.24 (0.86 to 1.78)
	Out of the workforce	263	14 (5.3)	1.4 (–1.5 to 4.2)	1.34 (0.78 to 2.31)	1.59 (0.93 to 2.73)
Income, quartiles	Lowest	1126	76 (6.8)	Ref	1	1
	Second	1127	60 (5.3)	–1.4 (–3.4 to 0.5)	0.79 (0.57 to 1.09)	0.81 (0.59 to 1.13)
	Third	1126	60 (5.3)	–1.4 (–3.4 to 0.6)	0.79 (0.57 to 1.10)	0.91 (0.66 to 1.26)
	Highest	1127	59 (5.2)	–1.5 (–3.5 to 0.4)	0.78 (0.56 to 1.08)	0.81 (0.57 to 1.15)
Number of chronic diseases	0	1994	84 (4.2)	Ref	1	1
	1 or 2	2085	134 (6.4)	2.2 (0.8 to 3.6)	1.53 (1.17 to 1.99)	1.08 (0.83 to 1.40)
	≥ 3	439	38 (8.7)	4.4 (1.7 to 7.2)	2.05 (1.42 to 2.97)	1.17 (0.75 to 1.82)
Reason for encounter (ICPC–2)	A: General and unspecified	416	37 (8.9)	Ref	1	1
	B: Blood, blood forming organs	39	8 (20.5)	11.6 (–1.3 to 24.6)	2.31 (1.16 to 4.60)	2.45 (1.22 to 4.92)
	D: Digestive	218	33 (15.1)	6.2 (0.8 to 11.7)	1.70 (1.10 to 2.64)	1.85 (1.19 to 2.89)
	F: Eye	43	1 (2.3)	–6.6 (–11.8 to –1.3)	0.26 (0.04 to 1.86)	0.34 (0.05 to 2.37)
	H: Ear	71	1 (1.4)	–7.5 (–11.4 to –3.6)	0.16 (0.02 to 1.14)	0.18 (0.03 to 1.30)
	K: Cardiovascular	561	17 (3.0)	–5.9 (–8.9 to –2.8)	0.34 (0.19 to 0.60)	0.26 (0.15 to 0.44)
	L: Musculoskeletal	819	27 (3.3)	–5.6 (–8.6 to –2.6)	0.37 (0.23 to 0.60)	0.43 (0.26 to 0.70)
	N: Neurological	174	7 (4.0)	–4.9 (–8.9 to –0.9)	0.45 (0.21 to 0.99)	0.52 (0.23 to 1.15)
	P: Psychological	501	7 (1.4)	–7.5 (–10.4 to –4.6)	0.16 (0.07 to 0.35)	0.21 (0.09 to 0.47)
	R: Respiratory	492	37 (7.5)	–1.4 (–5.0 to 2.2)	0.85 (0.55 to 1.31)	0.91 (0.55 to 1.50)
	S: Skin	464	28 (6.0)	–2.9 (–6.3 to 0.6)	0.68 (0.42 to 1.09)	0.86 (0.54 to 1.37)
	T: Endocrine/metabolic	193	6 (3.1)	–5.8 (–9.5 to –2.1)	0.35 (0.15 to 0.81)	0.29 (0.13 to 0.63)
	U: Urinary tract	136	9 (6.6)	–2.3 (–7.3 to 0.3)	0.74 (0.37 to 1.50)	0.73 (0.34 to 1.56)
	W: Pregnancy, contraception	116	3 (2.6)	–6.3 (–10.3 to –2.3)	0.29 (0.09 to 0.93)	0.84 (0.25 to 2.87)
	X: Female genital	187	25 (13.4)	4.5 (–1.1 to 10.1)	1.50 (0.93 to 2.42)	2.82 (1.69 to 4.72)
	Y: Male genital	55	10 (18.2)	9.3 (–1.3 to 19.8)	2.04 (1.08 to 3.87)	1.84 (0.97 to 3.49)
	Z: Social problems	33	0 (0)	—	—	—

^aPrevalence of suspicion: 60.2 (mean), 18–97 (min–max), 17.5 (SD). ^bAdjusted for sex, age group, chronic disease group, income quartile, and clustering. ^cAge: 51 years (mean), 18–100 years (min–max), 18.6 (SD). ICPC–2 = International Classification of Primary Care, second edition. SD = standard deviation.

Table 2. GPs' actions following consultation prompted by suspicion of serious disease

		Suspicion present (n = 256), n (%)	No suspicion (n = 4262), n (%)	Univariate, PR (95% CI)	Multivariate, ^a PR (95% CI)
Referral	All referrals	134 [52.3]	878 [20.6]	2.54 [2.23 to 2.90]	2.56 [2.22 to 2.96]
	Outpatient clinic	40 [15.6]	207 [4.9]	3.22 [2.35 to 4.40]	3.27 [2.34 to 4.56]
	Hospital admission	9 [3.5]	45 [1.1]	3.33 [1.65 to 6.74]	3.17 [1.54 to 6.50]
	Primary care specialist	28 [10.9]	215 [5.0]	2.17 [1.49 to 3.15]	2.35 [1.65 to 3.33]
	Diagnostic imaging	43 [16.8]	181 [4.2]	3.96 [2.91 to 5.38]	3.95 [2.80 to 5.57]
	Others ^b	25 [9.8]	299 [7.0]	1.39 [0.94 to 2.05]	1.45 [0.98 to 2.16]
Tests in GP clinic ^c		140 [54.7]	1744 [40.9]	1.34 [1.19 to 1.50]	1.29 [1.16 to 1.44]
Follow-up in general practice	Scheduled follow-up	162 [63.3]	2082 [48.9]	1.30 [1.18 to 1.42]	1.15 [1.05 to 1.26]
	New contact if needed	33 [12.9]	876 [20.6]	0.63 [0.46 to 0.87]	0.69 [0.50 to 0.95]
	No follow-up scheduled	43 [16.8]	1011 [23.7]	0.71 [0.54 to 0.93]	0.78 [0.59 to 1.03]
	Missing	18 [7.0]	293 [6.9]		

^aPR (prevalence ratio) adjusted for sex, age group, chronic disease group, income quartile, and clustering. ^bSuch as physiotherapist, laboratory, psychologist, or dentist.

^cSuch as blood samples or urine analysis.

[95% CI = 3.0 to 9.0] and an HR of 4.69 [95% CI = 2.51 to 8.75] after 2 months, and a PPV of 7.4% [95% CI = 4.5 to 11.3] and an HR of 1.13 [95% CI = 0.45 to 2.85] after 6 months (data not shown).

The proportions of patients using the different healthcare services after the index consultation are seen in Table 4. The use of GP, primary-care specialist, and diagnostic imaging increased, especially in the 2-month period after the index consultation. Use of hospital services (inpatient and outpatient) remained increased after 2 months. Results were not altered when analysing the number of GP visits instead

of the proportion of patients who had a GP consultation (data not shown).

Exclusion of individuals with missing information on suspicion did not significantly change any results.

DISCUSSION

Summary

In nearly 6% of all consultations in general practice, the GP had a suspicion of cancer or another serious disease. Higher age and presentation of symptoms from the digestive system, blood or blood-forming organs, or female genitals were associated with suspicion of serious disease. A suspicion

Table 3. Risk of serious disease after index consultation and predictive values of suspicion

	Time after index consultation, months	Risk time, months	Suspicion present, n	No suspicion, n	Univariate HR (95% CI)	Multivariate ^a HR (95% CI)	PPV (95% CI)	NPV (95% CI)	Prevalence, %
All diagnoses of serious disease	0–2	8853.6	25	122	3.54 (2.30 to 5.45)	2.98 (1.93 to 4.62)	9.8 (6.4 to 14.1)	97.2 (96.6 to 97.6)	3.2
	2–6	17 060.5	17	157	2.00 (1.21 to 3.30)	1.52 (0.92 to 2.53)	16.4 (12.1 to 21.5) ^b	93.5 (92.7 to 94.2) ^b	7.1 ^b
New diagnoses of cancer	0–2	8853.6	6	10	10.42 (3.79 to 28.67)	7.55 (2.66 to 21.39)	2.3 (0.9 to 5.0)	99.8 (99.6 to 99.9)	0.4
	2–6	17 060.5	2	12	3.08 (0.69 to 13.78)	1.82 (0.40 to 8.29)	3.1 (1.4 to 6.1) ^b	99.5 (99.2 to 99.7) ^b	0.7 ^b
New diagnoses of another serious disease	0–2	8853.6	19	112	2.93 (1.80 to 4.77)	2.51 (1.53 to 4.11)	7.4 (4.5 to 11.3)	97.4 (96.9 to 97.9)	2.9
	2–6	17 060.5	15	145	1.91 (1.12 to 3.25)	1.49 (0.87 to 2.54)	13.3 (9.4 to 18.1) ^b	94.0 (93.2 to 94.7) ^b	6.4 ^b

^aHR adjusted for age (continuous), sex, and chronic disease (dichotomous). ^bPrevalence: 0–6 months. HR = hazard ratio. NPV = negative predictive value. PPV = positive predictive value.

Table 4. Use of healthcare services after index consultation, by GP suspicion

	Time after consultation, months	Suspicion present (n = 256) n (%)	No suspicion (n = 4262) n (%)	Univariate RR (95% CI)	Adjusted ^a RR (95% CI)
GP consultation	0–2	172 (67.2)	2522 (59.2)	1.13 (1.04 to 1.24)	1.14 (1.06 to 1.24)
	2–6	132 (51.6)	2159 (50.6)	1.03 (0.91 to 1.16)	0.99 (0.88 to 1.11)
Primary care specialists	0–2	43 (16.8)	406 (9.5)	1.77 (1.33 to 2.36)	1.73 (1.32 to 2.26)
	2–6	31 (12.1)	425 (10.0)	1.23 (0.88 to 1.73)	1.20 (0.86 to 1.68)
All hospital visits	0–2	95 (37.1)	714 (16.8)	2.22 (1.87 to 2.64)	1.90 (1.62 to 2.23)
	2–6	93 (36.3)	982 (23.0)	1.60 (1.35 to 1.90)	1.40 (1.19 to 1.63)
Hospital admission	0–2	43 (16.8)	258 (6.1)	2.78 (2.07 to 3.75)	1.98 (1.49 to 2.63)
	2–6	43 (16.8)	354 (8.3)	2.05 (1.53 to 2.74)	1.62 (1.24 to 2.12)
Outpatient clinic visits	0–2	81 (31.6)	604 (14.2)	2.24 (1.84 to 2.72)	1.99 (1.66 to 2.40)
	2–6	78 (30.5)	872 (20.5)	1.51 (1.25 to 1.84)	1.34 (1.11 to 1.62)
All diagnostic imaging ^b	0–2	66 (25.8)	472 (11.1)	2.33 (1.87 to 2.92)	1.71 (1.27 to 2.29)
	2–6	55 (21.5)	679 (15.9)	1.37 (1.07 to 1.74)	1.11 (0.81 to 1.52)
X-ray ^b	0–2	40 (15.6)	243 (5.7)	2.75 (2.02 to 3.75)	2.08 (1.53 to 2.81)
	2–6	34 (13.3)	335 (7.9)	1.71 (1.23 to 2.38)	1.29 (0.94 to 1.77)
Ultrasound ^b	0–2	30 (11.7)	239 (5.6)	2.10 (1.47 to 3.00)	1.89 (1.32 to 2.70)
	2–6	28 (10.9)	362 (8.5)	1.30 (0.91 to 1.88)	1.20 (0.84 to 1.72)
CT or MRI scanning ^b	0–2	23 (9.0)	72 (1.7)	5.33 (3.39 to 8.38)	3.76 (2.37 to 5.98)
	2–6	20 (7.8)	143 (3.4)	2.36 (1.51 to 3.71)	1.51 (0.98 to 2.34)
Endoscopies	0–2	17 (6.6)	59 (1.4)	4.81 (2.85 to 8.13)	3.76 (2.22 to 6.38)
	2–6	18 (7.0)	89 (2.1)	3.42 (2.09 to 5.58)	2.90 (1.77 to 4.75)

^aAdjusted for sex, age group, chronic disease group, income quartile and use of relevant variable in the preceding year (dichotomous). ^bProcedures performed at hospitals and by practising specialists. CT = computerised tomography. MRI = magnetic resonance imaging. RR = relative risk.

increased the risk of having a test performed or being referred for further investigation. In particular, the use of diagnostic imaging and endoscopies was increased after the index consultation. The risk of receiving a new diagnosis of cancer or other serious disease increased, particularly within the first 2 months after the index consultation, and the PPV of GP suspicion was 9.8% within the first 2 months and 16.4% within 6 months after the consultation.

Strengths and limitations

The major strengths of this study are the prospective design and the high number of consecutive consultations at randomly assigned working days in a non-selected group of patients. Further, the ability to link the registered patients with national registries is an additional strength. The authors believe the risk of Hawthorne effect is minimal because the question on suspicion only formed a small part of a larger registration form and GPs were informed only that this study concerned

disease and symptoms patterns, along with activities in general practice.

One limitation is that GPs did not register the patient's personal identification numbers in 525 of the consultations (10.4%), (Figure 1). This omission occurred among specific GPs as a consequence of their principles of confidentiality; it is likely that these omissions did not bias the results.

Another limitation was missing information about suspicion. These contacts were included in the 'no-suspicion' group to preserve statistical power and because the researchers considered it plausible that GPs would rarely miss this question if they did have a suspicion. The sociodemographic characteristics of these patients was similar to that of those in the 'no-suspicion' group and excluding patients with missing data on suspicion from the analyses did not alter the results as there was no reason to believe that this principle is associated with the association between suspicion and future healthcare use and diagnoses.

A further limitation was that 53.6% of the invited GPs chose not to participate. However, the researchers have no reason to believe that this influences the association between suspicion and subsequent diagnosis.

Serious diseases diagnosed and managed in general practice were not included as serious disease was identified in the Danish National Registry of Patients, which includes only hospital diagnoses. However, it is only rarely that serious disease of relevance to this study does not include hospitalisation.

The authors did not know whether the diagnosed serious disease was directly associated with the recorded consultation, but 52.4% (22 of 42) of the patients in whom a suspicion was confirmed had a reason for encounter that was related to the subsequent diagnosis. It remains unknown whether the 22% with a reason for encounter that was related to the later diagnosis, but in whom GPs had no suspicion, represent neglected seriousness of disease as there is no information on possible subsequent consultations. This lack of information on patient courses is also important to consider when noting that for 87.0% (279 of 321, Table 3) those diagnosed with serious disease, this was not suspected by the GPs.

Another possible source of information bias was the lack of definition of serious diseases. The number of serious diseases defined and identified in the hospital registry influenced the prevalence of serious disease and, hence, caused the PPV to change from 9.8% to 5.5% when including only definite serious diseases. Nevertheless, this is still of a magnitude that corresponds with the most important alarm symptoms. The effect on the HR of including more diseases was less predictable because of possible differential misclassifications. The HRs increased from 2.98 to 4.69, indicating that the inclusion of more diseases caused an underestimation of the associations between suspicion and serious disease.

Comparison with existing literature

The high frequency of symptoms of potentially serious disease is challenging for GPs if they are to identify patients for further investigation.²¹ This is confirmed by the findings of Ingebrigtsen *et al* and Scheel *et al*, who found that warning signs of cancer were present in 12.4%⁸ of all GP consultations and that suspicion was raised in only 24%⁹ of these consultations. However, these figures cannot be compared with the 5.7% found in this study as the authors of the former studies only asked for information on suspicion if a warning sign

was present, whereas this study inquired whether there was a suspicion of cancer or another serious disease for all patients seen.^{8,9} The authors believe that this proportion of 5.7% illustrates the actual load of serious disease suspicion in GPs' daily work.

In this study, the PPV of a GP suspicion (9.8%) corresponds well with the PPVs of cancer alarm symptoms and the 7.8% found in Nylenna's study;¹³ however, the present study included various other serious diseases as well as cancer. Shapley *et al* reviewed the literature on PPVs of cancer alarm symptoms and signs in general practice and found that only nine symptoms and signs had PPVs of more than 5%.⁷ A specific level of PPV prompting referral cannot be established, but studies indicate that levels above 1% should prompt investigation.^{4,7} As in the study by Scheel *et al*,⁹ 6.2% (279 of 4518) of the patients in the current study were diagnosed with a serious disease without the GP having a suspicion of one being present after the index consultation.

The increased use of referrals and diagnostic tests among patients where the GP had a suspicion is in line with the findings by Scheel *et al*.⁹ This emphasises that support for further investigation initiated by GPs is crucial when a suspicion emerges.²² The importance of GPs' suspicion has also been highlighted by Hamilton and the fact that most patients start their diagnostic pathway for cancer in primary care.^{6,23} GPs depend on relevant secondary care investigations in order to, most often, reject that the cause of symptoms is cancer or another serious disease.

Implications for practice

The present study confirms that action should be taken when the GP suspects serious disease; PPVs are relatively high, and the healthcare system should support this investigation by providing access to, for example, imaging and endoscopies. The UK and Denmark have organised cancer investigation as a fast-track system (for example, 2-week wait referrals) that requires patients to present with specific alarm symptoms to qualify for immediate referral. However, as many patients in general practice present with vague or unspecific symptoms, GP access to relevant and speedy diagnostic investigations is crucial. Organisation of the primary diagnostic pathways and how to support GPs should be a main focus in future studies in this area.

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Ethical approval

The project was approved by the Danish Data Protection Agency (J.no. 2008-41-2195 and J.no. 2009-41-3471) and by the Danish Health and Medicines Agency (J.no. 7-604-04-2/49/EHE). According to Danish law, approval from the National Committee on Health Research Ethics was not required as no biomedical intervention was performed.

Provenance

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Competing interests

The authors have declared no competing interests.

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