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Lifestyle, socioeconomic status and healthcare seeking with gynaecological cancer alarm symptoms – A population based study

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Complete List of Authors:	Balasubramaniam, Kirubakaran; Research Unit of General Practice, Department of Public Health, University of Southern Denmark Elnegaard, Sandra; Research Unit of General Practice, Department of Public Health, University of Southern Denmark Rasmussen, Sanne; Research Unit of General Practice, Department of Public Health, University of Southern Denmark Haastrup, Peter; Research Unit of General Practice, Department of Public Health, University of Southern Denmark Christensen, René; Research Unit of General Practice, Department of Public Health, University of Southern Denmark Søndergaard, Jens; Research Unit of General Practice, Department of Public Health, University of Southern Denmark Jربول, Dorte; Research Unit of General Practice, Department of Public Health, University of Southern Denmark
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2 1 **Lifestyle, socioeconomic status and healthcare seeking with gynaecological cancer**
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4 2 **alarm symptoms – A population based study**
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10 4 Kirubakaran Balasubramaniam¹, Sandra Elnegaard¹, Sanne Rasmussen¹, Peter Fentz Haastrup¹, René dePont Christensen¹, Jens
11 5 Søndergaard¹, Dorte Ejg Jarbøl¹
12 6

13
14
15 7 ¹Research Unit of General Practice, Department of Public Health, University of Southern Denmark, Tel +45 6550 3830, J.B.
16 8 Winsløvs Vej 9A, 5000 Odense C, Denmark
17
18 9

19
20 10 **Corresponding author:**

21
22 11 Kirubakaran Balasubramaniam

23
24 12 J.B. Winsløvs Vej 9A

25
26 13 5000 Odense C

27
28 14 Denmark

29
30 15 Telephone: +45 6550 3739

31
32 16 kiruba@health.sdu.dk
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19 Abstract

20 Objectives: To determine the proportion of contacts to general practitioner (GP) with recent onset
21 gynaecological cancer alarm symptoms (pelvic pain, postmenopausal bleeding, bleeding during intercourse
22 or pain during intercourse) and to analyse the associations between lifestyle factors, socioeconomic status
23 and GP contact for these symptoms.

24 Design: Cross-sectional survey combined with data from national registers.

25 Setting: The general Danish population.

26 Participants: A total of 25 866 non-pregnant women ≥ 20 years completed the survey. Women reporting at
27 least one of four gynaecological alarm symptoms within the preceding six months form the study base (N =
28 2957).

29 Results: The proportion of women reporting GP contact ranged from 21.1% (pain during intercourse) to
30 32.6% (postmenopausal bleeding). Women aged 60+ years had higher odds of reporting GP contact for at
31 least one of the four gynaecological cancer alarm symptoms compared to those aged 20-39 years (OR 2.56,
32 95%-CI: 1.69 – 3.89), and immigrants had higher odds of reporting GP contact for at least one of the
33 symptoms (OR 1.56, 95%-CI: 1.13-2.15) compared to ethnic Danish individuals.

34 Among those reporting postmenopausal bleeding and/or bleeding during intercourse, women in the age
35 group 60+ years had higher odds of reporting GP contact compared to those aged 20-39 years (OR 2.79,
36 95%-CI: 1.33 – 5.87). A high educational level (>12 years) was positively associated with reporting GP
37 contact for postmenopausal bleeding and/or bleeding during intercourse compared to a low educational level
38 (<10 years) (OR 2.23, 95%-CI: 1.19 – 4.19).

39 No associations were found with lifestyle factors.

40 Conclusions: Few women contacted their GP with recent onset gynaecological cancer alarm symptoms.

41 Higher age, being immigrant and higher educational level increased the odds of GP contact. Future studies
42 should explore the reasons for these findings as this may aid in prompting early diagnosis and thereby
43 improve the prognosis of gynaecological cancer.

1
2 44 **Keywords:** Gynaecological cancer; symptoms; lifestyle; socioeconomic status; healthcare seeking

3
4 45 **Strengths and limitations of this study**

- 5 46 • The population is large, which enables investigation of small subgroups.
6 47 • Socio-economic data are obtained from national registers of high quality.
7 48 • Telephone interviews enabled additional responses from individuals who are usually rarely represented in surveys.
8 49 • GP contacts are seen in relation to experienced symptoms, thus reflecting true actions rather than hypothetical
9 50 situations.
10 51 • Data regarding GP contacts are self-reported and thus may be prone to bias.
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53 INTRODUCTION

54 Several studies have shown that late stage cancer diagnosis is associated with reduced survival¹⁻³. This is
55 also the case for gynaecological cancer, and timely diagnosis and treatment are thus considered essential for
56 prognosis.

57 For most patients, the diagnostic process is still initiated based on a symptom presentation, although some
58 patients are diagnosed through screening programmes⁴. The time period from the first symptom to diagnosis
59 consists of several intervals, and each of these intervals contributes to the overall time spent in the diagnostic
60 process⁵. To reduce both the patient interval and the diagnostic interval⁵, several countries have
61 implemented referral guidelines and organizational changes^{6,7}. Most of these guidelines suggest that
62 individuals presenting with symptoms indicative of cancer (alarm symptoms) should be urgently referred to
63 specialized investigative trajectories.

64 A prerequisite for the GP to refer to specialized investigations is, however, that individuals contact the GP
65 when experiencing symptoms. Evidently, not all symptom experiences lead to healthcare seeking⁸⁻¹⁰, and
66 several parameters might affect the decision to contact a GP with symptoms, such as socioeconomic status
67¹¹, experience with illness¹², and lifestyle factors (e.g., smoking status, alcohol intake, and body mass index
68 (BMI)¹³⁻¹⁵. Specifically, studies show that sociodemographic factors are associated with prolonged time to
69 diagnosis for a number of other cancers, while an unhealthy lifestyle is associated with longer intervals prior
70 to diagnosis¹⁶⁻¹⁸ including gynaecological cancers¹⁹. An enhanced understanding of the healthcare seeking
71 behaviour with gynaecological cancer alarm symptoms in different groups in the general population might
72 improve policy interventions targeting early diagnosis of gynaecological cancer.

73
74 Therefore the aims of this study were 1) to determine the proportion of women in the general population
75 reporting recent onset of gynaecological cancer alarm symptoms with subsequent GP contact and 2) to
76 analyse the associations between lifestyle factors, socioeconomic status and contact to GP with
77 gynaecological cancer alarm symptoms.

78 METHODS

1 79 The study was conducted as a nationwide combined questionnaire and register-based study. It is a part of a
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3
4 80 larger study, the Danish Symptom Cohort (DaSC), that investigates the prevalence of symptom experiences
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6 81 and healthcare seeking behaviour in the general population²⁰. In Denmark, 98% of citizens are listed with a
7
8 82 GP who serves as a gatekeeper for access to specialist care in either a hospital setting or in private practice.
9
10 83 The Danish healthcare system is tax-funded and provides free medical care for all in both primary care and
11
12 84 hospital setting²¹.

15 85 **Study subjects**

18 86 For the survey (DaSC), a random sample of 100 000 adults aged 20 years or older was drawn from the
19
20 87 Danish Civil Registration System (CRS), in which all Danish citizens are registered with a unique
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22 88 identification number. This identification number enables accurate linkage between national registers. The
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24 89 sampling procedure did not include individuals who had indicated in the CRS that they did not want to
25
26 90 participate in research-related inquiries. Of the 100 000 invited individuals, 51 090 (51.1%) were women,
27
28 91 and only data for the women are included in this paper.

32 92 **The questionnaire**

35 93 The questionnaire was designed using the internet-based platform SurveyXact, and the invited individuals
36
37 94 received a unique 12-digit login by postal letter²². This login had to be entered on a secure webpage in order
38
39 95 to access the questionnaire. In order to prevent exclusion of people with no internet access, the participants
40
41 96 were offered to complete the survey by telephone interview. Questionnaire data were collected from June to
42
43 97 December 2012.

46 98 The development of the questionnaire followed standardized and widely recognized procedures and was
47
48 99 pilot-tested in its entirety for content validity, relevance, acceptability and feasibility. The final version of
49
50 100 the questionnaire was field-tested on 500 individuals, randomly sampled from the CRS prior to the survey.
51
52
53 101 The data quality, response rate, floor and ceiling effects, score ranges of single items and scores were

1
2 102 assessed. Additional details about the design of the study and the data collection process are described
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4 103 elsewhere²⁰.

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6
7 104 A comprehensive questionnaire concerning the experience of 44 predefined specific and nonspecific cancer
8
9 105 alarm symptoms, as well as general and frequent symptoms, was developed. The alarm symptoms were
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11 106 selected based on a review of literature including national and international cancer referral guidelines²³⁻²⁷.
12
13 107 This study focuses on four symptoms (pelvic pain, postmenopausal bleeding, pain during intercourse and
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15 108 bleeding after intercourse), as these are mentioned in cancer referral guidelines regarding gynaecological
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17 109 cancer^{24 25}. The respondents were asked whether they had experienced one or more of the symptoms within
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19
20 110 the preceding four weeks, when they had experienced the first onset of the symptom(s), and whether they
21
22 111 had contacted a GP about the symptom(s). The wording of the question regarding symptoms was: "Have you
23
24 112 experienced any of the following bodily sensations, symptoms, or discomforts within the past four weeks?
25
26 113 (Yes/no)" A follow up question for reported symptoms was phrased: "When did you experience these for the
27
28 114 first time? (Less than a month ago/1-3 months ago/3-6 months ago/More than 6 months ago)". The question
29
30 115 regarding contacting a GP was: "Have you contacted your GP concerning the symptom(s) you have
31
32 116 experienced within the preceding four weeks, through appointment, by telephone or email? (Yes/no)". The
33
34 117 questionnaire also included items about self-reported lifestyle factors, such as smoking habits and alcohol
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36 118 consumption. Besides, the respondents reported their height and weight.

40 119 **Register data**

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42
43 120 Information about socioeconomic status (SES) and demographics was obtained from Statistics Denmark for
44
45 121 each individual using the unique personal identification number in the CRS. Statistics Denmark is a
46
47 122 governmental institution responsible for collecting and handling data from a number of social and
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49 123 administrative registers²⁸. Information about educational level, household income, labour market affiliation,
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51 124 cohabitation status and ethnicity was obtained via data linkage to this database for each respondent for the
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53
54 125 year 2011, the year before the survey.

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57 126

127 **Statistical analysis**

128 In order to explore how recently onset symptoms were managed, symptoms with onset more than six months
129 ago were excluded. As pregnant women may display a different healthcare seeking behaviour compared to
130 non-pregnant women, individuals who stated that they were pregnant within the preceding six months were
131 excluded from the analyses (Figure 1).

132 The proportions of women with recent onset of gynaecological symptoms and contact with a GP are
133 presented as percentages for each symptom. Confidence intervals were calculated using binomial
134 distribution. Logistic regression models were used to calculate unadjusted and adjusted odds ratios (ORs) for
135 associations between GP contact with at least one of the four cancer alarm symptoms and each of the
136 covariates. A sub-analysis was performed for those reporting postmenopausal bleeding and/or bleeding
137 during intercourse, as these symptoms from a clinical perspective are considered as especially alarming thus
138 prompting fast referral and investigation. The variables considered for analyses were age group, smoking
139 status, alcohol consumption, body mass index (BMI), educational level, income, labour market affiliation,
140 cohabitation status and ethnicity. All these were categorical, and if they showed a significant association
141 with GP contact in the crude logistic analyses, they were included in the subsequent logistic regression
142 models.

143 Age was categorized as follows: 20–39, 40–59 or 60+ years old. The BMI was calculated for each
144 respondent who was then categorized as underweight ($BMI < 18.5$), normal weight ($18.5 \leq BMI < 25$),
145 overweight ($25 \leq BMI < 30$) or obese ($BMI \geq 30$) according to the WHO guidelines²⁹. Smoking status was
146 categorized as never-smokers, former smokers or current smokers. Alcohol consumption was categorized
147 according to average intake (measured in units): 0, 1–7 units/week or > 8 units/week. Education was
148 categorized according to the highest attained educational level: low (<10 years, i.e. primary and lower
149 secondary school); middle (10–12 years, i.e. vocational education and upper secondary school); or high (>12
150 years, i.e. short-, medium- or long-term higher education)³⁰. Equivalence-weighted disposable income was
151 categorized as low income (1st quartile), middle income (2nd and 3rd quartiles) or high income (4th

quartile). The equivalent disposable income comprises all income (wages, salaries, benefits and pensions) after taxation for the entire household and is adjusted for number of persons in the household³¹. Labour market affiliation was categorized as currently working, pensioner or out of the workforce. Cohabitation status was categorized as cohabiting/married or single. Ethnicity was categorized as people of Danish origin, immigrants or descendants of immigrants.

All statistical tests used a significance level of $p < 0.05$. Data analyses were conducted using STATA statistical software 13.1 (StataCorp, College Station, TX, USA).

RESULTS

A total of 26 466 women completed the questionnaire, yielding a response rate of 54.5% for the women. The median age of the participants was 51 years (interquartile range 39–63) compared to 53 years (interquartile range 37–71) for non-participants. A total of 600 (2.3%) stated that they had been pregnant within the preceding six months and were thus excluded from the analyses. A total of 2 957 (11.4%) of the remaining 25 866 women reported at least one gynaecological cancer alarm symptom with onset within the preceding six months, Figure 1.

The descriptive data for the study population are shown in Table 1. The proportion of respondents reporting GP contact ranged from 21.1% for pain during intercourse to 32.6% for postmenopausal bleeding, Table 2.

		All respondents, n (%)	Symptomatic women, n (%)
Total		25 866 (100.0)	2 957 (100.0)
Age groups			
	20-39	6 151 (23.8)	1 390 (47.0)
	40-59	11 078 (42.8)	1 290 (43.6)
	60+	8 637 (33.4)	277 (9.4)
BMI			
	Underweight (BMI<18.5)	625 (2.4)	87 (2.9)
	Normal weight (18.5≤BMI<25)	13 552 (52.4)	1 628 (55.1)
	Overweight (25≤BMI<30)	6 933 (26.8)	724 (24.5)
	Obese (BMI ≥ 25)	3 571 (13.8)	402 (13.6)
Smoking status			
	Never smokers	12 151 (47.0)	1 384 (46.8)

	Former smokers	7 571 (29.3)	752 (25.4)
	Current smokers	5 044 (19.5)	714 (24.1)
Alcohol consumption			
	0 units/week	7 738 (29.9)	1 056 (35.7)
	1-7 units/week	12 828 (49.6)	1 405 (47.5)
	>8 units/week	5 300 (20.5)	496 (16.8)
Labour market affiliation			
	Working	17 265 (66.7)	2 406 (81.4)
	Pensions	5 943 (23.0)	172 (5.8)
	Out of workforce	2 636 (10.2)	375 (12.7)
Equivalence weighted disposable income			
	Lowest group (1 st quartile)	4 478 (17.3)	659 (22.3)
	Middle group (2 nd and 3 rd quartile)	13 527 (52.3)	1 602 (54.2)
	Highest group (4 th quartile)	7 816 (30.2)	686 (23.2)
Ethnicity			
	Danish	24 150 (93.4)	2 728 (92.3)
	Immigration	1 555 (6.0)	196 (6.6)
	Descendants of immigrants	116 (0.4)	23 (0.8)
Marital status			
	Single	7 127 (27.6)	839 (28.4)
	Married/cohabiting	18 694 (72.3)	2 108 (71.3)
Educational level			
	Low (<10 years)	5 172 (20.0)	486 (16.4)
	Middle (10-12 years)	10 819 (41.8)	1 330 (45.0)
	High (>12 years)	9 207 (35.6)	1 054 (35.6)

*Reporting at least one gynaecological cancer alarm symptom within the preceding six months

168

Symptom	Symptom experiences, n	Contact to GP, n (%)
Pelvic pain	2 184	486 (22.3)
Postmenopausal bleeding	190	62 (32.6)
Pain during intercourse	867	183 (21.1)
Bleeding during intercourse	347	90 (25.9)
At least one of the abovementioned symptoms	2 957	683 (23.1)
Postmenopausal bleeding and/or bleeding during intercourse	523	147 (28.1%)

169

170 Among individuals reporting at least one of the four cancer alarm symptoms, no significant association with
 171 GP contact was found for BMI, smoking status, alcohol consumption, household income, educational level

172 or marital status. Thus, the variables included in the adjusted logistic model were age group, labour market
 173 affiliation and ethnicity. In the full model, we observed that women in the age group 60+ years had higher
 174 odds of reporting GP contact compared to the youngest age group (OR 2.56, 95%-CI: 1.69 – 3.89).
 175 Likewise, immigrants had higher odds of reporting GP contact (OR 1.56, 95%-CI: 1.13-2.15) compared to
 176 ethnic Danish individuals, Table 3.

Table 3: Crude and adjusted ORs for associations between lifestyle factors, socioeconomic status and contact to GP with at least one of the four cancer alarm symptoms (symptom experiences < 6 months)

Age group	Crude ORs			Adjusted ORs ^a		
	OR	p-value	95%-CI	OR	p-value	95%-CI
20-39	1.00	.	1.00-1.00	1.00	.	1.00-1.00
40-59	1.11	0.284	0.92-1.33	1.13	0.198	0.94-1.36
60+	1.91	<0.001	1.45-2.53	2.56	<0.001	1.69-3.89
Smoking status						
Never smoker	1.00	.	1.00-1.00			
Former smoker	1.04	0.699	0.85-1.28			
Current smoker	0.93	0.533	0.75-1.16			
BMI						
Underweight	1.00	.	1.00-1.00			
Normal weight	1.43	0.209	0.82-2.48			
Overweight	1.22	0.497	0.69-2.16			
Obese	1.21	0.532	0.67-2.18			
Alcohol consumption						
0	1.00	.	1.00-1.00			
1-7	0.97	0.730	0.80-1.17			
>8	1.03	0.830	0.80-1.32			
Labour market affiliation						
Working	1.00	.	1.00-1.00	1.00	.	1.00-1.00
Pensions	1.49	0.022	1.06-2.09	0.64	0.089	0.38-1.07
Out of workforce	1.04	0.786	0.80-1.34	0.92	0.523	0.70-1.20
Equivalence weighted disposable income						
Low (1 st quartile)	1.00	.	1.00-1.00			
Middle (2 nd and 3 rd quartile)	0.97	0.784	0.78-1.20			
High (4 th quartile)	1.07	0.582	0.83-1.38			
Ethnicity						
Danish	1.00	.	1.00-1.00	1.00	.	1.00-1.00
Immigrants	1.52	0.010	1.10-2.08	1.56	0.007	1.13-2.15
Descendants of immigrants	0.95	0.927	0.35-2.58	1.06	0.913	0.39-2.87
Marital status						

	Single	1.00	.	1.00-1.00		
	Married/living together	0.99	0.892	0.82-1.19		
Educational level						
	Low (<10 years)	1.00	.	1.00-1.00		
	Middle (10-12 years)	0.88	0.322	0.69-1.13		
	High (>12 years)	0.89	0.362	0.69-1.14		

^a: Adjusted for age, labour market affiliation and ethnicity

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178 In the subgroup analyses among women reporting postmenopausal bleeding and/or bleeding during
 179 intercourse, we found no associations with GP contact for smoking status, BMI, alcohol consumption, labour
 180 market affiliation, household income, ethnicity or marital status. Women aged 60+ had higher odds of
 181 reporting GP contact compared to women in the age group 20-39 (OR 2.79, 95%-CI: 1.33 – 5.87).
 182 Furthermore, those with a high educational level (>12 years) had higher odds of reporting GP contact
 183 compared to those with a low educational level (< 10 years) (OR 2.23, 95%-CI: 1.19 – 4.19), Table 4.

Table 4: Crude and adjusted ORs for associations between lifestyle factors, socioeconomic status and contact to GP with postmenopausal bleeding and/or bleeding during intercourse (symptom experiences < 6 months)

		Crude ORs			Adjusted ORs ^b		
		OR	p-value	95%-CI			
Age group							
	20-39	1.00	.	1.00-1.00	1.00	.	1.00-1.00
	40-59	1.32	0.189	0.87-1.98	1.35	0.166	0.88-2.05
	60+	2.75	0.005	1.36-5.56	2.79	0.007	1.33-5.87
Smoking status							
	Never smoker	1.00	.	1.00-1.00			
	Former smoker	1.30	0.271	0.82-2.07			
	Current smoker	0.95	0.843	0.59-1.54			
BMI							
	Underweight	1.00	.	1.00-1.00			
	Normal weight	1.69	0.358	0.55-5.22			
	Overweight	1.38	0.592	0.43-4.42			
	Obese	1.82	0.335	0.54-6.14			
Alcohol consumption							
	0	1.00	.	1.00-1.00	1.00	.	1.00-1.00
	1-7	1.02	0.932	0.65-1.60	0.97	0.887	0.60-1.56
	≥8	1.78	0.035	1.04-3.05	1.52	0.141	0.87-2.67
Labour market affiliation							
	Working	1.00	.	1.00-1.00			
	Pensions	1.43	0.434	0.58-3.49			
	Out of workforce	0.72	0.294	0.39-1.33			
Equivalence weighted disposable income							

	Low (1 st quartile)	1.00	.	1.00-1.00			
	Middle (2 nd and 3 rd quartile)	1.32	0.288	0.79-2.19			
	High (4 th quartile)	1.35	0.299	0.77-2.35			
Ethnicity							
	Danish	1.00	.	1.00-1.00			
	Immigrants	0.95	0.885	0.46-1.95			
	Descendants of immigrants	2.59	0.344	0.36-18.55			
Marital status							
	Single	1.00	.	1.00-1.00			
	Married/living together	1.06	0.783	0.71-1.58			
Educational level							
	Low (<10 years)	1.00	.	1.00-1.00	1.00	.	1.00-1.00
	Middle (10-12 years)	1.32	0.359	0.73-2.39	1.54	0.170	0.83-2.87
	High (>12 years)	2.01	0.023	1.10-3.67	2.23	0.012	1.19-4.19

^b : Adjusted for age, alcohol consumption and educational level

184

185 DISCUSSION

186 Main findings

187 In this nationwide study comprising 26 466 women from the general Danish population, 23.1% of those
 188 reporting four specific gynaecological alarm symptoms with onset less than six months prior had contacted a
 189 GP with at least one of the symptoms. The proportion of GP contacts ranged from 21.1% (pain during
 190 intercourse) to 32.6% (postmenopausal bleeding).

191 Women in the oldest age group and immigrants had significantly higher odds of having contacted the GP
 192 when reporting at least one of the four symptoms. No associations were found with smoking status, BMI,
 193 alcohol consumption, labour market affiliation, household income, marital status or educational level. In the
 194 subgroup analysis of women reporting postmenopausal bleeding and/or bleeding during intercourse, higher
 195 age and a high educational level were associated with having contacted the GP. In this subgroup, no
 196 associations were found with labour market affiliation, household income, ethnicity, marital status or any
 197 lifestyle factors.

198

199 **Study strengths and limitations**

200 Strengths of this study include the large study sample (51 090 women) and the relatively high response rate
201 (54.5% among women). An overall responder analysis of the entire study cohort including both genders
202 showed that respondents were more often cohabiting, had higher educational level, had higher income, were
203 of Danish origin and more were affiliated with the workforce¹⁰.

204 In Denmark, detailed socioeconomic and demographic data on an individual level are available, based on
205 administrative data, and defined in Statistics Denmark^{30 31}. The quality of these data is in general high and
206 there is a low risk of misclassification²⁸.

207 This study is based on self-reported GP contacts and symptoms with onset less than six months prior to
208 questionnaire distribution. Even though this time span is relatively short, some memory decay cannot be
209 ruled out, which may result in underreporting of both symptoms and GP contacts. On the other hand, some
210 individuals may have felt that the alarm symptoms should have led to GP contact, which may have resulted
211 in some extent of desirability bias.

212 Furthermore, it is important to keep in mind that the lifestyle factors (alcohol consumption, smoking status
213 and BMI) are self-reported and may be underreported, thus prone to information bias. However, it has been
214 demonstrated that self-reported anthropometric data are reliable – especially among young people^{32 33}.

216 **Comparison with existing literature**

217 It has been demonstrated that women lack knowledge about symptoms of gynaecological cancer and that
218 they often attribute the symptoms to benign conditions³⁴, increasing age and simply being a woman³⁵. In
219 hypothetical situations of experiencing gynaecological cancer alarm symptoms, many women hesitate to
220 seek medical attention³⁶. Our study confirms that this is also the case when actually experiencing
221 gynaecological alarm symptoms in real life.

1
2 222 Few studies have investigated the associations between healthcare seeking and lifestyle and
3
4 223 sociodemography of individuals reporting gynaecological alarm symptoms. In a survey by Brain et al.,
5
6 224 anticipated delay for women put in the hypothetical situation of experiencing gynaecological alarm
7
8 225 symptoms was associated with lower educational level³⁶. The different results in our study may be due to
9
10 226 the fact that Brain et al. explores a hypothetical situation with rather vague symptoms, compared to our study
11
12 227 with truly experienced symptoms that are more specific of nature. Another study based on the DaSC-survey
13
14 228 has demonstrated that healthcare seeking with respiratory symptoms is significantly lower among smokers
15
16 229³⁷. This may be caused by smokers being more aware of the connection between their lifestyle and their
17
18 230 symptoms, which may lead to negligence of symptoms, fear of stigmatization etc. In our study, we did not
19
20 231 find such an association, which may indicate that the relationship between lifestyle and gynaecological alarm
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22 232 symptoms is less apparent, thus preventing any differences in healthcare seeking among individuals with
23
24 233 different lifestyles.
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31 235 **Interpretation of findings**

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33 236 We evaluated whether social inequity existed with regard to GP contact with gynaecological alarm
34
35 237 symptoms, and whether lifestyle influenced the healthcare seeking process. In the Danish healthcare system,
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37 238 GPs act as gatekeepers and healthcare coordinators for their patients. A prerequisite for further investigations
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39 239 is, however, that patients seek healthcare when experiencing symptoms. We have demonstrated that
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41 240 healthcare seeking with gynaecological cancer alarm symptoms is positively associated with age, ethnicity
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43 241 and educational level. As the risk of cancer increases with age for both endometrial and ovarian cancer,
44
45 242 higher proportions of healthcare seeking in the older age groups may be beneficial for detecting these
46
47 243 cancers. On the other hand, cervical cancer is also frequently occurring among younger women, and means
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49 244 to promote more appropriate healthcare seeking in the younger age groups must be explored. This study
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51 245 found that higher educational level was positively associated with increased healthcare seeking, while no
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53 246 significant associations were found for lifestyle factors. This might indicate that educational level is a proxy
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1
2 247 for health literacy, and that the latter is the determining factor for healthcare related actions rather than
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4 248 lifestyle. In a previous study, we found that higher educational level was positively associated with specialist
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6 249 investigation of gynaecological symptoms³⁸. When taking the results of the present study into account, the
7
8 250 social inequality in healthcare utilization may be even more profound than previously expected. As we found
9
10 251 no associations with lifestyle factors, a central point of interest for researchers, clinicians and policy makers
11
12 252 should be the influence of sociodemographic factors on timely diagnosis of symptomatic individuals.
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15 253

18 254 **CONCLUSION**

21 255 Less than one third of women contact their GP with newly onset gynaecological cancer alarm symptoms.
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23 256 Higher age, being immigrant and a higher educational level increased the odds of GP contact. Especially the
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25 257 effect of educational level may contribute to social inequality in healthcare utilization. Future studies should
26
27 258 explore the reasons for these findings, and in the meanwhile, clinicians should be aware of patients at risk of
28
29 259 not seeking help with symptoms, e.g. younger women or women with short education.
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31

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39
40 263 Diagnosis in Primary Care (CaP).
41
42

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44
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46

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49 267 manuscript.
50

52 268 **DISCLOSURE OF INTERESTS**

55 269 The authors have nothing to declare.
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2 270 **DETAILS OF ETHICS APPROVAL**
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4
5 271 The participants in the study were informed that there would be no clinical follow-up, and that they should
6
7 272 contact their GP with any concerns or questions. The Regional Scientific Ethics Committee for Southern
8
9 273 Denmark was notified prior to the survey and had no concerns regarding this project. The project was
10
11 274 approved by the Danish Data Protection Agency (journal no. 2011-41-6651).
12

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15

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20

21
22 278 **DATA SHARING STATEMENT**
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25 279 The datasets generated and analysed during the current study are not publicly available due to the data
26
27 280 protection regulations of the Danish Data Protection, Statistics Denmark and the Danish Health and
28
29 281 Medicines Authority. Access to data is strictly limited to the researchers who have obtained permission for
30
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32
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35
36 284 **CONTRIBUTORSHIP STATEMENT**
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38
39 285 KB, SE, SR and DJ participated in the design of the study, development of the questionnaire, the logistics
40
41 286 concerning the survey and the drafting of the manuscript. KB moreover did the main work in forming the
42
43 287 manuscript and carried out the statistical analyses. JS participated in the design of the study, development of
44
45 288 the questionnaire and drafting of the manuscript. RdC participated in the statistical considerations
46
47 289 concerning the survey and analyses. PFH participated in the interpretation of the findings and drafting of the
48
49 290 manuscript. All authors read and approved the final manuscript.
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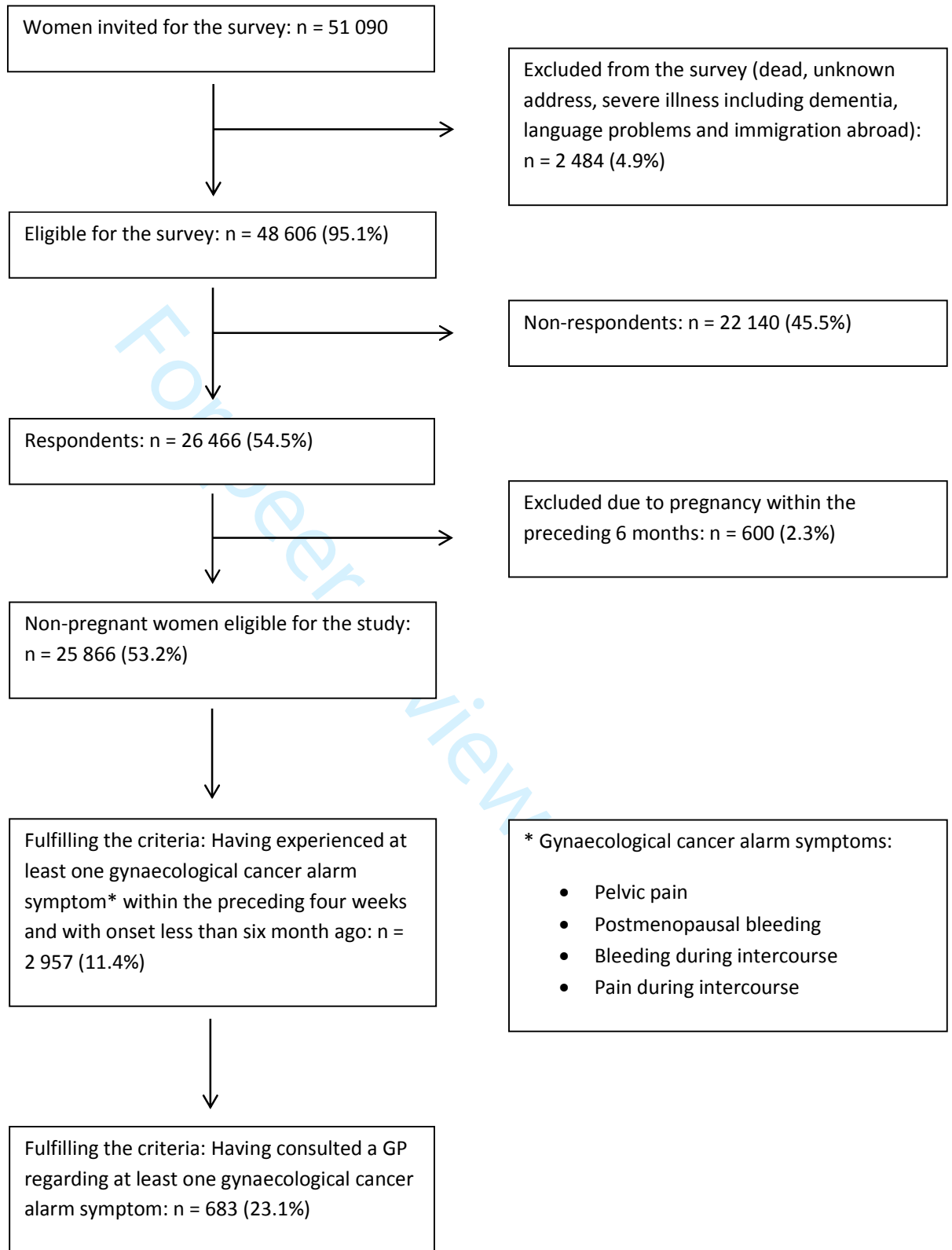
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Figure 1: Study population



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2 1 **Lifestyle, socioeconomic status and healthcare seeking among women with**
3 2 **gynaecological cancer alarm symptoms – A combined questionnaire- and register based**
4 3 **population study**

5 4 Kirubakaran Balasubramaniam¹, Sandra Elnegaard¹, Sanne Rasmussen¹, Peter Fentz Haastrup¹, René dePont Christensen¹, Jens
6 5 Søndergaard¹, Dorte Ejg Jarbøl¹

7 6
8 7 ¹Research Unit of General Practice, Department of Public Health, University of Southern Denmark, Tel +45 6550 3830, J.B.
9 8 Winsløvs Vej 9A, 5000 Odense C, Denmark

10 9
11 10 **Corresponding author:**

12 11 Kirubakaran Balasubramaniam

13 12 J.B. Winsløvs Vej 9A

14 13 5000 Odense C

15 14 Denmark

16 15 Telephone: +45 6550 3739

17 16 kiruba@health.sdu.dk

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Abstract

Objectives: To determine the proportion of contacts to general practitioner (GP) with recent onset gynaecological cancer alarm symptoms (pelvic pain, postmenopausal bleeding, bleeding during intercourse or pain during intercourse) and to analyse the associations between lifestyle factors, socioeconomic status and GP contact for these symptoms.

Design: Cross-sectional survey combined with data from national registers.

Setting: The general Danish population.

Participants: A total of 25 866 non-pregnant women ≥ 20 years completed the survey. Women reporting at least one of four gynaecological alarm symptoms within the preceding six months form the study base (N = 2957).

Results: The proportion of women reporting GP contact ranged from 21.1% (pain during intercourse) to 32.6% (postmenopausal bleeding). Women aged 60+ years had higher odds of reporting GP contact for at least one of the four gynaecological cancer alarm symptoms compared to those aged 20-39 years (OR 2.56, 95%-CI: 1.69 – 3.89), and immigrants had higher odds of reporting GP contact for at least one of the symptoms (OR 1.56, 95%-CI: 1.13-2.15) compared to ethnic Danish individuals.

Among those reporting postmenopausal bleeding and/or bleeding during intercourse, women in the age group 60+ years had higher odds of reporting GP contact compared to those aged 20-39 years (OR 2.79, 95%-CI: 1.33 – 5.87). A high educational level (>12 years) was positively associated with reporting GP contact for postmenopausal bleeding and/or bleeding during intercourse compared to a low educational level (<10 years) (OR 2.23, 95%-CI: 1.19 – 4.19).

No associations were found with lifestyle factors.

Conclusions: Few women contacted their GP with recent onset gynaecological cancer alarm symptoms.

Higher age, being immigrant and higher educational level increased the odds of GP contact. Future studies should explore the reasons for these findings as this may aid in prompting early diagnosis and thereby improve the prognosis of gynaecological cancer.

1
2 44 **Keywords:** Gynaecological cancer; symptoms; lifestyle; socioeconomic status; healthcare seeking

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4 45 **Strengths and limitations of this study**

- 5 46 • The population is large, which enables investigation of small subgroups.
6 47 • Socio-economic data are obtained from national registers of high quality.
7 48 • Telephone interviews enabled additional responses from individuals who are usually rarely represented in surveys.
8 49 • GP contacts are seen in relation to experienced symptoms, thus reflecting true actions rather than hypothetical
9 50 situations.
10 51 • Data regarding GP contacts are self-reported and thus may be prone to bias.
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53 INTRODUCTION

54 Several studies have shown that late stage cancer diagnosis is associated with reduced survival¹⁻³. This is
55 also the case for gynaecological cancer, and timely diagnosis and treatment are thus considered essential for
56 prognosis.

57 For most patients, the diagnostic process is still initiated based on a symptom presentation, although some
58 patients are diagnosed through screening programmes⁴. The time period from the first symptom to diagnosis
59 consists of several intervals, and each of these intervals contributes to the overall time spent in the diagnostic
60 process⁵. To reduce both the patient interval and the diagnostic interval⁵, several countries have
61 implemented referral guidelines and organizational changes^{6,7}. Most of these guidelines suggest that
62 individuals presenting with symptoms indicative of cancer (alarm symptoms) should be urgently referred to
63 specialized investigative trajectories. Some of the symptoms mentioned in guidelines are commonly
64 occurring and often caused by benign conditions⁸, which poses a clinical challenge due to the rather modest
65 positive predictive values for cancer. On the other hand, most of the cancers must be detected among
66 symptomatic individuals⁴, which justifies the approach with fast track investigations. Some of the symptoms
67 are suggested investigated even when presented as single symptoms, e.g. postmenopausal bleeding, whereas
68 others, e.g. pain during intercourse, are rather considered as alarm symptoms in combination with other
69 symptoms.

70 A prerequisite for the GP to refer to specialized investigations is, however, that individuals contact the GP
71 when experiencing symptoms. Evidently, not all symptom experiences lead to healthcare seeking⁹⁻¹¹, and
72 several parameters might affect the decision to contact a GP with symptoms, such as socioeconomic status
73¹², experience with illness¹³, and lifestyle factors (e.g., smoking status, alcohol intake, and body mass index
74 (BMI)¹⁴⁻¹⁶. Specifically, studies show that sociodemographic factors are associated with prolonged time to
75 diagnosis for a number of other cancers, while an unhealthy lifestyle is associated with longer intervals prior
76 to diagnosis¹⁷⁻¹⁹ including gynaecological cancers²⁰. An enhanced understanding of the healthcare seeking
77 behaviour with gynaecological cancer alarm symptoms in different groups in the general population might
78 improve policy interventions targeting early diagnosis of gynaecological cancer.

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4 80 Therefore, the aims of this study were 1) to determine the proportion of women in the general population
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6 81 reporting recent onset of gynaecological cancer alarm symptoms with subsequent GP contact and 2) to
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8 82 analyse the associations between lifestyle factors, socioeconomic status and contact to GP with
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10 83 gynaecological cancer alarm symptoms.

11 84 **METHODS**

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15 85 The study was conducted as a nationwide combined questionnaire and register-based study. It is a part of a
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17 86 larger study, the Danish Symptom Cohort (DaSC), that investigates the prevalence of symptom experiences
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19 87 and healthcare seeking behaviour in the general population²¹. In Denmark, 98% of citizens are listed with a
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21 88 GP. The GPs have a gatekeeping role in the health care system and with the exception of very few
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23 89 situations, patients do not have direct access to secondary care nor to specialist care in primary care. The
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25 90 Danish healthcare system is tax-funded and provides free medical care for all in both primary care and
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27 91 hospital setting²².

28 29 30 31 92 **Study subjects**

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34 93 For the survey (DaSC), a random sample of 100 000 adults aged 20 years or older was drawn from the
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36 94 Danish Civil Registration System (CRS), in which all Danish citizens are registered with a unique
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38 95 identification number. This identification number enables accurate linkage between national registers. The
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40 96 sampling procedure did not include individuals who had indicated in the CRS that they did not want to
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42 97 participate in research-related inquiries. Of the 100 000 invited individuals, 51 090 (51.1%) were women,
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44 98 and only data for the women are included in this paper.

45 46 47 48 99 **The questionnaire**

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51 100 The questionnaire was designed using the internet-based platform SurveyXact, and the invited individuals
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53 101 received a unique 12-digit login by postal letter²³. This login had to be entered on a secure webpage in order
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55 102 to access the questionnaire. In order to prevent exclusion of people with no internet access, the participants

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2 103 were offered to complete the survey by telephone interview. Questionnaire data were collected from June to
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4 104 December 2012.

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7 105 The development of the questionnaire followed standardized and widely recognized procedures and was
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9 106 pilot-tested in its entirety for content validity, relevance, acceptability and feasibility. The final version of
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11 107 the questionnaire was field-tested on 500 individuals, randomly sampled from the CRS prior to the survey.
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13 108 The data quality, response rate, floor and ceiling effects, score ranges of single items and scores were
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15 109 assessed. Additional details about the design of the study and the data collection process are described
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17 110 elsewhere ²¹.

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20 111 A comprehensive questionnaire concerning the experience of 44 predefined specific and nonspecific cancer
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22 112 alarm symptoms, as well as general and frequent symptoms, was developed. The alarm symptoms were
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24 113 selected based on a review of literature including national and international cancer referral guidelines ²⁴⁻²⁸.
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26 114 This study focuses on four symptoms (pelvic pain, postmenopausal bleeding, pain during intercourse and
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28 115 bleeding after intercourse), as these are mentioned in cancer referral guidelines regarding gynaecological
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30 116 cancer ^{25 26}. The respondents were asked whether they had experienced one or more of the symptoms within
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32 117 the preceding four weeks, when they had experienced the first onset of the symptom(s), and whether they
33
34 118 had contacted a GP about the symptom(s). The wording of the question regarding symptoms was: "Have you
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36 119 experienced any of the following bodily sensations, symptoms, or discomforts within the past four weeks?
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38 120 (Yes/no)" A follow up question for reported symptoms was phrased: "When did you experience these for the
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40 121 first time? (Less than a month ago/1-3 months ago/3-6 months ago/More than 6 months ago)". The question
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42 122 regarding contacting a GP was: "Have you contacted your GP concerning the symptom(s) you have
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44 123 experienced within the preceding four weeks, through appointment, by telephone or email? (Yes/no)". The
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46 124 questionnaire also included items about self-reported lifestyle factors, such as smoking habits and alcohol
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48 125 consumption. Respondents also reported their height and weight.

52 53 54 126 **Patient and public involvement**

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2 127 Individuals from the general population only participated in the pilot- and field testing of the questionnaire,
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4 128 and were otherwise not involved in the design of the study, research questions or other aspects of the survey,
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6 129 including recruitment and conduct of the study. The results of the study will be disseminated to the public by
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8 130 summaries in popular scientific magazines.
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11 131 **Register data**

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14 132 Information about socioeconomic status (SES) and demographics was obtained from Statistics Denmark for
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16 133 each individual using the unique personal identification number in the CRS. Statistics Denmark is a
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18 134 governmental institution responsible for collecting and handling data from a number of social and
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20 135 administrative registers²⁹. Information about educational level, household income, labour market affiliation,
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22 136 cohabitation status and ethnicity was obtained via data linkage to this database for each respondent for the
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24 137 year 2011, the year before the survey.
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30 139 **Statistical analysis**

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34 140 In order to explore how recently onset symptoms were managed, symptoms with onset more than six months
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36 141 ago were excluded. As pregnant women may display a different healthcare seeking behaviour compared to
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38 142 non-pregnant women, individuals who stated that they were pregnant within the preceding six months were
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40 143 excluded from the analyses (Figure 1).
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42

43 144 The proportions of women with recent onset of gynaecological symptoms and contact with a GP are
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45 145 presented as percentages for each symptom. Confidence intervals were calculated using binomial
46
47 146 distribution. Logistic regression models were used to calculate unadjusted and adjusted odds ratios (ORs) for
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49 147 associations between GP contact with at least one of the four cancer alarm symptoms and each of the
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51 148 covariates. A sub-analysis was performed for those reporting postmenopausal bleeding and/or bleeding
52
53 149 during intercourse, as these symptoms from a clinical perspective are considered as especially alarming thus
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55 150 prompting fast investigation. The variables considered for analyses were age group, smoking status, alcohol
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1 151 consumption, body mass index (BMI), educational level, income, labour market affiliation, cohabitation
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3
4 152 status and ethnicity. All these were categorical, and if they showed a significant association with GP contact
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6 153 in the crude logistic analyses, they were included in the subsequent logistic regression models.
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9 154 Age was categorized as follows: 20–39, 40–59 or 60+ years old. The BMI was calculated for each
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11 155 respondent who was then categorized as underweight ($BMI < 18.5$), normal weight ($18.5 \leq BMI < 25$),
12
13 156 overweight ($25 \leq BMI < 30$) or obese ($BMI \geq 30$) according to the WHO guidelines³⁰. Smoking status was
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15 157 categorized as never-smokers, former smokers or current smokers. Alcohol consumption was categorized
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17 158 according to average intake (measured in units): 0, 1–7 units/week or > 8 units/week. Education was
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19 159 categorized according to the highest attained educational level: low (<10 years, i.e. primary and lower
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21 160 secondary school); middle (10–12 years, i.e. vocational education and upper secondary school); or high (>12
22
23 161 years, i.e. short-, medium- or long-term higher education)³¹. Equivalence-weighted disposable income was
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25 162 categorized as low income (1st quartile), middle income (2nd and 3rd quartiles) or high income (4th
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27 163 quartile). The equivalent disposable income comprises all income (wages, salaries, benefits and pensions)
28
29 164 after taxation for the entire household and is adjusted for number of persons in the household³². Labour
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31 165 market affiliation was categorized as currently working, pensioner or out of the workforce. Cohabitation
32
33 166 status was categorized as cohabiting/married or single. Ethnicity was categorized as people of Danish origin,
34
35 167 immigrants (individuals not born in Denmark by parents who holding Danish citizenships) or descendants of
36
37 168 immigrants (individuals born in Denmark by parents who are neither born in Denmark nor holding Danish
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39 169 citizenships).
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44 170 All statistical tests used a significance level of $p < 0.05$. Data analyses were conducted using STATA
45
46 171 statistical software 13.1 (StataCorp, College Station, TX, USA).
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49 172 RESULTS

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52 173 A total of 26 466 women completed the questionnaire, yielding a response rate of 54.5% for the women. The
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54 174 median age of the participants was 51 years (interquartile range 39–63) compared to 53 years (interquartile
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56 175 range 37–71) for non-participants. A total of 600 (2.3%) stated that they had been pregnant within the
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176 preceding six months and were thus excluded from the analyses. A total of 2 957 (11.4%) of the remaining
 177 25 866 women reported at least one gynaecological cancer alarm symptom with onset within the preceding
 178 six months, Figure 1.

179 The descriptive data for the study population are shown in Table 1. The proportion of respondents reporting
 180 GP contact ranged from 21.1% for pain during intercourse to 32.6% for postmenopausal bleeding, Table 2.

Table 1: Descriptive data for the study population

	All respondents, n (%)	Symptomatic women, n (%)
Total	25 866 (100.0)	2 957 (100.0)
Age groups		
20-39	6 151 (23.8)	1 390 (47.0)
40-59	11 078 (42.8)	1 290 (43.6)
60+	8 637 (33.4)	277 (9.4)
BMI		
Underweight (BMI<18.5)	625 (2.4)	87 (2.9)
Normal weight (18.5≤BMI<25)	13 552 (52.4)	1 628 (55.1)
Overweight (25≤BMI<30)	6 933 (26.8)	724 (24.5)
Obese (BMI ≥ 25)	3 571 (13.8)	402 (13.6)
Smoking status		
Never smokers	12 151 (47.0)	1 384 (46.8)
Former smokers	7 571 (29.3)	752 (25.4)
Current smokers	5 044 (19.5)	714 (24.1)
Alcohol consumption		
0 units/week	7 738 (29.9)	1 056 (35.7)
1-7 units/week	12 828 (49.6)	1 405 (47.5)
>8 units/week	5 300 (20.5)	496 (16.8)
Labour market affiliation		
Working	17 265 (66.7)	2 406 (81.4)
Pensions	5 943 (23.0)	172 (5.8)
Out of workforce	2 636 (10.2)	375 (12.7)
Equivalence weighted disposable income		
Lowest group (1 st quartile)	4 478 (17.3)	659 (22.3)
Middle group (2 nd and 3 rd quartile)	13 527 (52.3)	1 602 (54.2)
Highest group (4 th quartile)	7 816 (30.2)	686 (23.2)
Ethnicity		
Danish	24 150 (93.4)	2 728 (92.3)
Immigration	1 555 (6.0)	196 (6.6)
Descendants of immigrants	116 (0.4)	23 (0.8)
Marital status		
Single	7 127 (27.6)	839 (28.4)
Married/cohabiting	18 694 (72.3)	2 108 (71.3)

Educational level			
	Low (<10 years)	5 172 (20.0)	486 (16.4)
	Middle (10-12 years)	10 819 (41.8)	1 330 (45.0)
	High (>12 years)	9 207 (35.6)	1 054 (35.6)

*Reporting at least one gynaecological cancer alarm symptom within the preceding six months

181

Table 2: Gynaecological cancer alarm symptoms within the preceding six months, and self-reported contact to GP

Symptom	Symptom experiences, n	Contact to GP, n (%)
Pelvic pain	2 184	486 (22.3)
Postmenopausal bleeding	190	62 (32.6)
Pain during intercourse	867	183 (21.1)
Bleeding during intercourse	347	90 (25.9)
At least one of the abovementioned symptoms	2 957	683 (23.1)
Postmenopausal bleeding and/or bleeding during intercourse	523	147 (28.1%)

182

183 Among individuals reporting at least one of the four cancer alarm symptoms, no significant association with
 184 GP contact was found for BMI, smoking status, alcohol consumption, household income, educational level
 185 or marital status. Thus, the variables included in the adjusted logistic model were age group, labour market
 186 affiliation and ethnicity. In the full model, we observed that women in the age group 60+ years had higher
 187 odds of reporting GP contact compared to the youngest age group (OR 2.56, 95%-CI: 1.69 – 3.89).
 188 Likewise, immigrants had higher odds of reporting GP contact (OR 1.56, 95%-CI: 1.13-2.15) compared to
 189 ethnic Danish individuals, Table 3.

Table 3: Crude and adjusted ORs for associations between lifestyle factors, socioeconomic status and contact to GP with at least one of the four cancer alarm symptoms (symptom experiences < 6 months)

		Crude ORs			Adjusted ORs ^a		
		OR	p-value	95%-CI	OR	p-value	95%-CI
Age group	20-39	1.00	.	1.00-1.00	1.00	.	1.00-1.00
	40-59	1.11	0.284	0.92-1.33	1.13	0.198	0.94-1.36
	60+	1.91	<0.001	1.45-2.53	2.56	<0.001	1.69-3.89
Smoking status	Never smoker	1.00	.	1.00-1.00			
	Former smoker	1.04	0.699	0.85-1.28			
	Current smoker	0.93	0.533	0.75-1.16			

10

BMI							
	Underweight	1.00	.	1.00-1.00			
	Normal weight	1.43	0.209	0.82-2.48			
	Overweight	1.22	0.497	0.69-2.16			
	Obese	1.21	0.532	0.67-2.18			
Alcohol consumption							
	0	1.00	.	1.00-1.00			
	1-7	0.97	0.730	0.80-1.17			
	>8	1.03	0.830	0.80-1.32			
Labour market affiliation							
	Working	1.00	.	1.00-1.00	1.00	.	1.00-1.00
	Pensions	1.49	0.022	1.06-2.09	0.64	0.089	0.38-1.07
	Out of workforce	1.04	0.786	0.80-1.34	0.92	0.523	0.70-1.20
Equivalence weighted disposable income							
	Low (1 st quartile)	1.00	.	1.00-1.00			
	Middle (2 nd and 3 rd quartile)	0.97	0.784	0.78-1.20			
	High (4 th quartile)	1.07	0.582	0.83-1.38			
Ethnicity							
	Danish	1.00	.	1.00-1.00	1.00	.	1.00-1.00
	Immigrants	1.52	0.010	1.10-2.08	1.56	0.007	1.13-2.15
	Descendants of immigrants	0.95	0.927	0.35-2.58	1.06	0.913	0.39-2.87
Marital status							
	Single	1.00	.	1.00-1.00			
	Married/living together	0.99	0.892	0.82-1.19			
Educational level							
	Low (<10 years)	1.00	.	1.00-1.00			
	Middle (10-12 years)	0.88	0.322	0.69-1.13			
	High (>12 years)	0.89	0.362	0.69-1.14			

^a: Adjusted for age, labour market affiliation and ethnicity

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191 In the subgroup analyses among women reporting postmenopausal bleeding and/or bleeding during
 192 intercourse, we found no associations with GP contact for smoking status, BMI, alcohol consumption, labour
 193 market affiliation, household income, ethnicity or marital status. Women aged 60+ had higher odds of
 194 reporting GP contact compared to women in the age group 20-39 (OR 2.79, 95%-CI: 1.33 – 5.87).
 195 Furthermore, those with a high educational level (>12 years) had higher odds of reporting GP contact
 196 compared to those with a low educational level (< 10 years) (OR 2.23, 95%-CI: 1.19 – 4.19), Table 4.

Table 4: Crude and adjusted ORs for associations between lifestyle factors, socioeconomic status and contact to GP with postmenopausal bleeding and/or bleeding during intercourse (symptom experiences < 6 months)

Age group	Crude ORs			Adjusted ORs ^b		
	OR	p-value	95%-CI			
20-39	1.00	.	1.00-1.00	1.00	.	1.00-1.00
40-59	1.32	0.189	0.87-1.98	1.35	0.166	0.88-2.05
60+	2.75	0.005	1.36-5.56	2.79	0.007	1.33-5.87
Smoking status						
Never smoker	1.00	.	1.00-1.00			
Former smoker	1.30	0.271	0.82-2.07			
Current smoker	0.95	0.843	0.59-1.54			
BMI						
Underweight	1.00	.	1.00-1.00			
Normal weight	1.69	0.358	0.55-5.22			
Overweight	1.38	0.592	0.43-4.42			
Obese	1.82	0.335	0.54-6.14			
Alcohol consumption						
0	1.00	.	1.00-1.00	1.00	.	1.00-1.00
1-7	1.02	0.932	0.65-1.60	0.97	0.887	0.60-1.56
≥8	1.78	0.035	1.04-3.05	1.52	0.141	0.87-2.67
Labour market affiliation						
Working	1.00	.	1.00-1.00			
Pensions	1.43	0.434	0.58-3.49			
Out of workforce	0.72	0.294	0.39-1.33			
Equivalence weighted disposable income						
Low (1 st quartile)	1.00	.	1.00-1.00			
Middle (2 nd and 3 rd quartile)	1.32	0.288	0.79-2.19			
High (4 th quartile)	1.35	0.299	0.77-2.35			
Ethnicity						
Danish	1.00	.	1.00-1.00			
Immigrants	0.95	0.885	0.46-1.95			
Descendants of immigrants	2.59	0.344	0.36-18.55			
Marital status						
Single	1.00	.	1.00-1.00			
Married/living together	1.06	0.783	0.71-1.58			
Educational level						
Low (<10 years)	1.00	.	1.00-1.00	1.00	.	1.00-1.00
Middle (10-12 years)	1.32	0.359	0.73-2.39	1.54	0.170	0.83-2.87
High (>12 years)	2.01	0.023	1.10-3.67	2.23	0.012	1.19-4.19

^b : Adjusted for age, alcohol consumption and educational level

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198 DISCUSSION

199 **Main findings**

200 In this nationwide study comprising 26 466 women from the general Danish population, 23.1% of those
201 reporting four specific gynaecological alarm symptoms with onset less than six months prior had contacted a
202 GP with at least one of the symptoms. The proportion of GP contacts ranged from 21.1% (pain during
203 intercourse) to 32.6% (postmenopausal bleeding).

204 Women in the oldest age group and immigrants had significantly higher odds of having contacted the GP
205 when reporting at least one of the four symptoms. No associations were found with smoking status, BMI,
206 alcohol consumption, labour market affiliation, household income, marital status or educational level. In the
207 subgroup analysis of women reporting postmenopausal bleeding and/or bleeding during intercourse, higher
208 age and a high educational level were associated with having contacted the GP. In this subgroup, no
209 associations were found with labour market affiliation, household income, ethnicity, marital status or any
210 lifestyle factors.

212 **Study strengths and limitations**

213 Strengths of this study include the large study sample (51 090 women) and the relatively high response rate
214 (54.5% among women). An overall responder analysis of the entire study cohort including both genders
215 showed that respondents were more often cohabiting, had higher educational level, had higher income, were
216 of Danish origin and more were affiliated with the workforce ¹¹.

217 In Denmark, detailed socioeconomic and demographic data on an individual level are available, based on
218 administrative data, and defined in Statistics Denmark ^{31 32}. The quality of these data is in general high and
219 there is a low risk of misclassification ²⁹.

220 Some of the symptoms mentioned in guidelines are frequently occurring in the general population, and
221 mostly caused by benign conditions e.g. normal menstrual cycle ⁸. As both the symptoms ³³ and

1
2 222 gynaecological cancers are age dependent³⁴, exploring the healthcare seeking for each symptom in different
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4 223 age groups would be of great value. However, some of the symptoms were somewhat rare and analysing
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6 224 these separately with regard to the explanatory variables would be in violation with Danish legislation and
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8 225 data protection regulations. In a previous study based on the same population cohort, increasing age was
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10 226 found to be significantly associated with healthcare seeking regardless of symptom type, supporting that our
11
12 227 finding regarding age may be due to other factors than the individual symptoms alone³⁵.

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15 228 This study is based on self-reported symptoms within a time frame of four weeks with onset less than six
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17 229 months prior to questionnaire distribution and GP contacts regarding these symptoms. Even though the time
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19 230 spans are relatively short, some memory decay cannot be ruled out, which may result in underreporting of
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21 231 both symptoms and GP contacts. On the other hand, some individuals may have felt that the alarm symptoms
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23 232 should have led to GP contact, which may have resulted in some extent of desirability bias. The time for GP
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25 233 contact was not specified as the intention was to obtain information on all GP contacts. Although some
26
27 234 respondents may have misunderstood the question, based on the pilot tests, we believe that the results are
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29 235 valid.

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33 236 Furthermore, it is important to keep in mind that the lifestyle factors (alcohol consumption, smoking status
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35 237 and BMI) are self-reported and may be underreported, thus prone to information bias. However, it has been
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37 238 demonstrated that self-reported anthropometric data are reliable – especially among young people^{36 37}.

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42 43 44 240 **Comparison with existing literature**

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47 241 It has been demonstrated that women lack knowledge about symptoms of gynaecological cancer and that
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49 242 they often attribute the symptoms to benign conditions³⁸, increasing age and simply being a woman³⁹. In
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51 243 hypothetical situations of experiencing gynaecological cancer alarm symptoms, many women hesitate to
52
53 244 seek medical attention⁴⁰. Our study confirms that this is also the case when actually experiencing
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55 245 gynaecological alarm symptoms in real life.

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2 246 Few studies have investigated the associations between healthcare seeking and lifestyle and
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4 247 sociodemography of individuals reporting gynaecological alarm symptoms. In a survey by Brain et al.,
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6 248 higher educational level was significantly associated with delay for women in the hypothetical situation of
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8 249 experiencing gynaecological alarm symptoms⁴⁰. The different results in our study may be due to the fact
9
10 250 that Brain et al. explores a hypothetical situation with rather vague symptoms, compared to our study with
11
12 251 truly experienced symptoms that are more specific of nature. In a study by Elliott et al., higher educational
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14 252 level was associated with higher degree of consulting the GP with both low- and high-impact symptoms, the
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16 253 tendency being more profound for high-impact symptoms. This supports our findings indicating that higher
17
18 254 educational level is indeed positively associated with healthcare seeking behaviour with gynaecological
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20 255 alarm symptoms of certain impact, as we only found the association for bleeding during intercourse and
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22 256 postmenopausal bleeding.
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26 257 Another study based on the DaSC-survey has demonstrated that healthcare seeking with respiratory
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28 258 symptoms is significantly lower among smokers⁴¹. This may be caused by the well-known association
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30 259 between smoking and respiratory symptoms, which may induce normalization of e.g. coughing among
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32 260 smokers. Likewise, smokers may experience other barriers towards healthcare-seeking such as fear of being
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34 261 blamed for their health conditions being caused by lifestyle. In our study, we did not find such an
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36 262 association, which may indicate that the association between lifestyle and healthcare seeking is specific for
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38 263 the symptoms in question and not generalizable to overall healthcare seeking.
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45 265 **Interpretation of findings**

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47 266 We evaluated whether social inequity existed with regard to GP contact with gynaecological alarm
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49 267 symptoms, and whether lifestyle influenced the healthcare seeking process. In the Danish healthcare system,
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51 268 GPs act as gatekeepers and healthcare coordinators for their patients. A prerequisite for further investigations
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53 269 is, however, that patients seek healthcare when experiencing symptoms. We have demonstrated that
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55 270 healthcare seeking with gynaecological cancer alarm symptoms is positively associated with age, ethnicity
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1
2 271 and educational level. As the risk of cancer increases with age for both endometrial and ovarian cancer,
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4 272 higher proportions of healthcare seeking in the older age groups may be beneficial for detecting these
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6 273 cancers. On the other hand, cervical cancer is also frequently occurring among younger women, and means
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8 274 to promote more appropriate healthcare seeking in the younger age groups must be explored, especially
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10 275 taking into consideration that adherence to cervical screening is lower among younger women ⁴². This study
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12 276 found that higher educational level was positively associated with increased healthcare seeking, while no
13
14 277 significant associations were found for lifestyle factors. This might indicate that educational level is a proxy
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16 278 for health literacy, and that the latter is the determining factor for healthcare related actions rather than
17
18 279 lifestyle. In a previous study, we found that higher educational level was positively associated with specialist
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20 280 investigation of gynaecological symptoms ⁴³. When taking the results of the present study into account, the
21
22 281 social inequality in healthcare utilization may be even more profound than previously expected. As we found
23
24 282 no associations with lifestyle factors, a central point of interest for researchers, clinicians and policy makers
25
26 283 should be the influence of sociodemographic factors on timely diagnosis of symptomatic individuals. At the
27
28 284 same time, it must be kept in mind that most of the symptoms are attributable to benign and often normal
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30 285 conditions which poses a challenge for both clinicians, the healthcare system and the symptomatic women
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32 286 who may be exposed to extensive investigations with the risk of iatrogenic harm and psychological distress.
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40 288 **CONCLUSION**

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43 289 Less than one third of women contact their GP with newly onset gynaecological cancer alarm symptoms.
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45 290 Higher age, being immigrant and a higher educational level increased the odds of GP contact. Especially the
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47 291 effect of educational level may contribute to social inequality in healthcare utilization. Future studies should
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49 292 explore the reasons for these findings, and in the meanwhile, clinicians should be aware of patients at risk of
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51 293 not seeking help with symptoms, e.g. younger women or women with lower education.
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1
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3
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5
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7

8
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10
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12

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14
15 301 manuscript.
16

17 18 302 **DISCLOSURE OF INTERESTS**

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21 303 The authors have nothing to declare.
22

23 24 304 **DETAILS OF ETHICS APPROVAL**

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26
27 305 The participants in the study were informed that there would be no clinical follow-up, and that they should
28
29 306 contact their GP with any concerns or questions. The Regional Scientific Ethics Committee for Southern
30
31 307 Denmark was notified prior to the survey and had no concerns regarding this project. The project was
32
33 308 approved by the Danish Data Protection Agency (journal no. 2011-41-6651).
34

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37
38
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40
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42

43 44 312 **DATA SHARING STATEMENT**

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47 313 The datasets generated and analysed during the current study are not publicly available due to the data
48
49 314 protection regulations of the Danish Data Protection, Statistics Denmark and the Danish Health and
50
51 315 Medicines Authority. Access to data is strictly limited to the researchers who have obtained permission for
52
53 316 data processing. This permission was granted to the Research Unit of General Practice, Department of Public
54
55 317 Health, University of Southern Denmark.
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1
2 318 **CONTRIBUTORSHIP STATEMENT**
3

4 319 KB, SE, SR and DJ participated in the design of the study, development of the questionnaire, the logistics
5
6 320 concerning the survey and the drafting of the manuscript. KB moreover did the main work in forming the
7
8 321 manuscript and carried out the statistical analyses. JS participated in the design of the study, development of
9
10 322 the questionnaire and drafting of the manuscript. RdC participated in the statistical considerations
11
12 323 concerning the survey and analyses. PFH participated in the interpretation of the findings and drafting of the
13
14 324 manuscript. All authors read and approved the final manuscript.
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18 325 **Figure 1: Study population**
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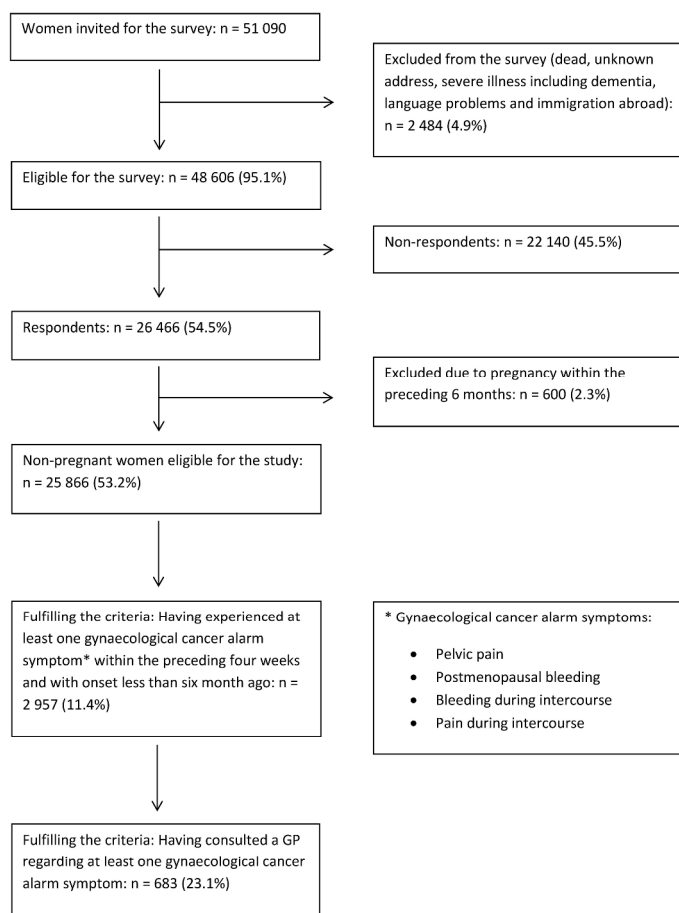
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Figure 1: Study population



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Figure 1: Study population
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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any pre-specified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-8
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-8
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	16, 17, 18
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7-8
		(b) Describe any methods used to examine subgroups and interactions	7-8
		(c) Explain how missing data were addressed	-
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	-

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9, Table 1
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	-
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	-
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Table 1
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 3 and 4
		(b) Report category boundaries when continuous variables were categorized	7-8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.