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Cervical cancer survivors and health care use: A Danish population-based register study

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HIGHLIGHTS

• Use of general practitioners, hospitals, and prescription drugs increased significantly after a cervical cancer diagnosis
• Use of psychologists/psychiatrists was unaffected by a cervical cancer diagnosis
• In five years after diagnosis, cervical cancer patients used on average analgesic/psychotropic drugs every 2–3 day
• Optimizing balance for cervical cancer patients between prescription drug use and psychologist support might be considered

Abstract

Objective. To evaluate the impact of a cervical cancer (CC) diagnosis on use of health care and prescription drugs.

Methods. This population-based register-study included Danish women aged 23–59 years and diagnosed with CC in 2001–2005. Women with a cervical screening outcome were used as comparison group. We obtained number of contacts to general practitioners (GPs), hospitals, psychologists/psychiatrists and defined daily doses (DDD) of analgesic/psychotropic prescription drugs. A difference-in-differences-design was used to estimate effect of a CC diagnosis on health-care use from five-year periods before and after the diagnosis/screening outcome.

Results. In total, 926 women with CC and 1,004,759 women without cancer were included. In five years following the date of CC diagnosis, CC patients had increased their use of GPs with 8.6 (95% CI 4.8–12.4) contacts more than women in the comparison group, and with 4.12 (95% CI 3.99–4.25) more hospital contacts. In contrast, use of psychologists/psychiatrists was low and largely unaffected by the CC diagnosis. For use of prescription drugs, analgesics increased with 80 (95% CI 60–100) DDD more in CC patients than in comparison women, and for psychotropics with 304 (95% CI 261–347) DDD more.

Conclusions. A CC diagnosis was followed by an increase in use of GPs, hospitals, and analgesic/psychotropic prescription drugs, while use of psychologist/psychiatrist was largely unaffected. This pattern may indicate that pain/mental health concerns after CC either persisted or were alleviated by other means only.

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1. Introduction

In Denmark, the cervical cancer incidence rate has decreased after cervical screening was introduced aiming to find and treat cervical lesions before progressing to cancer. In 1966, the age-standardized incidence rate was 33.8 per 100,000 (world standard population [W]) decreasing to 8.9 per 100,000 (W) in 2016 [1]. Nevertheless, still about 350 Danish women are diagnosed with cervical cancer every year and about 100 women die annually from the disease.

Cervical cancer treatment with surgery and radio-chemotherapy can induce permanent consequences e.g. urinary- and bowel problems, sexual- and vaginal problems, and menopausal symptoms [2]. Several
studies have reported on the risk of negative psychological consequences after diagnosis and treatment of cervical cancer [2–5]. Also, these patients were found to have a higher risk of reduced working ability, longer sick leave, and more often holding disability pension compared with the general population in the decades after the diagnosis [6,7]. In previous studies, early and late effects were assessed after the diagnoses of cervical cancer compared with a reference group. This does not allow control for a potential baseline differences between the patients and the reference group before the diagnosis.

On this basis, we undertook a population-based register study to evaluate the potential impact of a cervical cancer diagnosis on the patients’ use of health care services before and after their diagnosis. As health care indicators, we investigated contacts to general practitioners (GPs), hospitals, psychologists/psychiatrists, as well as the use of analgesic- and psychotropic prescription drugs. We hypothesized that women with cervical cancer increased their use of health care more than women without cancer.

2. Material and methods

2.1. Cervical cancer screening and cancer treatment in Denmark

In Denmark, the national screening guidelines were issued in 1986 recommending screening of women aged 23–59 years every third year. In 2007, the National Board of Health changed the recommendations to every third year for women aged 23–50, and every fifth year for women aged 50–65 years [8]. Conventional cytology was used nationwide until 2002 whereafter liquid-based cytology was gradually implemented and has been the standard technology since 2015 [9,10]. From 2007 onwards, high-risk HPV-testing has been used for triage of AS-CUS [11]; from 2012 onwards high-risk HPV-testing has been used as a check-out test in the screening program for women aged 60–64 years [12]; and from 1 January 2021 primary high-risk HPV screening with cytology triage will be used in a pilot period for half of women aged 30–59 years.

The treatment of cervical cancer is centralized to comparatively few cancer centers in Denmark and follows national evidence-based guidelines which are updated regularly and at least every third year [13]. Data was extracted during the years 2001–2005. Therefore, staging was based on FIGO 2000 [14]. According to the Danish guideline from 2002 [13], women with stage IA1 without vascular invasion were offered a conization. Women with stage IA1 and lymphovascular space invasion (LVSI), IA2, IB1 and IA with minor vaginal involvement underwent radical hysterectomy and pelvic lymphadenectomy. Women with stage IB-IVA as well as women with high-risk histopathological factors as lymph nodes metastases, parametrial invasion or resection margins were offered adjuvant radiotherapy. Palliative care was given to women with cervical cancer and distant metastases (stage IVB) [13]. Women were offered a total of ten follow-up appointments in the post-operative years; every third month during year 1, every sixth month during years 2 and 3, and annually years 4 and 5 [13].

2.2. Design

We conducted a population-based register study including all Danish women in screening age; 23–59 years old. For women in the cervical cancer group, we used the first-time cancer diagnosis in 2001–2005. As a comparison group, we selected women adherent to the screening program and who were not diagnosed with cervical cancer during the years 2001–2005 or before. As one-fifth of the cervical cancer cases included in the study was assumed to be stage IA1 [15] and therefore likely to have been diagnosed at screening, we used women undergoing screening as the comparison group. The index screening date considered for women in the comparison group was the first date of either a normal cytology or any non-malignant cervical abnormality including both cytological and histological diagnoses in 2001–2005. In both groups, we studied health-care use in a ten-year period from five years before the diagnosis—or index screening date to five years after. Mean number of contacts during the five years before diagnosis/screening outcome (“before”) was calculated as well as the mean number of contacts in total in the five years after diagnoses/screening outcome (“after”). The number of contacts before the diagnosis were included in order to control for differences in health care use already before the cervical cancer diagnosis. All included women had to be living in Denmark in all ten years and we thus required all subjects to survive for five years after the cancer surgery or the screening procedure. We allowed up to 1-month absence, which was likely a registration error.

As indicators of health care use, we used the number of contacts to GPs, to hospitals, both in- and out-patient contacts, as well as contacts to psychologists and/or psychiatrists. A single visit was calculated as one contact. We included all contacts observed, but the index operation date was excluded from the analysis. Also, we studied the use of prescription drugs of two groups; analgesic (ATC-code N02) and psychotropic prescription drugs (ATC N03, N05, N06, N07). We estimated numbers of “defined daily dose (DDD)” of the drugs. DDD is the assumed daily maintenance dose administered given to an adult for the drug’s main indication. Other variables were age and region. Age was stratified into three groups: 23–32 years, 33–42 years and 43–59 years. Residence areas were divided into three regions: “Capital”, “Islands”, and “Jutland”.

2.3. Data sources

In Denmark, all individuals with a permanent address receive a unique personal identification number (CPR-number). This number is used to link data from all the registers. All women diagnosed with cervical cancer are registered in the Danish Cancer Register, which is practically completed since its start in 1943 [16]. Cancers are now classified according to ICD10. Information on residence area, emigration, and vital status was retrieved from the Danish Civil Registration System [17]. We retrieved data on use of GP, psychologist and psychiatrist from the National Health Service Register [18] and use of in- and outpatient contacts to hospitals from the National Patient Register [19]. Purchased drugs in pharmacies were registered in the Danish National Prescription Registry which holds information on all prescribed and purchased drugs in Denmark [20]. The project was approved by the Danish Data Protection Agency (2010-41-5594).

2.4. Statistical analysis

We used the difference-in-differences method in which data provided 4 points of interest for each type of health care use; 1) number of contacts in the “before” period for women with cervical cancer, 2) number of contacts in the “before” period for women without cancer, 3) number of contacts in the “after” period for women with cancer, and 4) number of contacts in the “after” period for women without cancer. The aim of the analysis was to assess the effect of exposure, i.e. being diagnosed with cervical cancer, on the changes in the number of contacts and DDDs from the “before” to “after” period.

General linear mixed models and least square means were applied to the data and the mean number of contacts for women and DDDs for women with and without cervical cancer in the “before” and “after” period was computed. We also calculated the differences from the “before” to the “after” period for women with and without cancer, respectively. The confidence intervals of the means and of the difference in means with their statistical significance were calculated. Difference of differences were calculated using point estimates of the mean differences and the upper and lower confidence limit. We further repeated the analysis stratified by age and region. Analysis was performed using R, version 3.0.1 and SAS, version 9.4.
In total, 926 women with cervical cancer and 1,004,759 women without cancer were included in the study (Table 1). Cervical cancers consisted of 704 cases (76%) of squamous cell carcinomas, 185 cases (20%) of adenocarcinomas, and 37 (4%) unclassified cervical cancers. In the comparison group, normal cytology was diagnosed in 929,379 women (92.5%), abnormal diagnosis in 38,312 women (3.8%), and 35,884 had inadequate samples (3.6%).

The age distributions in the two groups differed (p < 0.001) (Table 1). More women with cervical cancer were aged 33–42 years (39%) compared with women without cancer (29%). The latter group was younger with more women aged 23–32 years old (22% vs. 29%, respectively). The distribution of women with and without cancer across regions was close to similar though slightly more women with cancer lived on the Islands (31% vs. 27%) and slightly more women without cancer lived in Jutland (46% vs. 51%) (p = 0.02).

### 3. Results

#### 3.1. Contacts to general practitioner

Contacts to GPs were common for both women with and without cervical cancer (Table 2). Women with cervical cancer had a mean number of 52.4 contacts to GPs in the “before” period and 66.5 in the “after” period, representing a change of 14.1 contacts (95% CI: 10.3–17.8) (Fig. 1). In women without cervical cancer, there was 55.2 contacts “before” and 60.6 “after” hence an increase of 5.5 contacts (95% CI: 5.3–5.6). Therefore, the number of contacts to GPs increased with 8.6 more contacts (95% CI: 4.8–12.4) for women with than without cancer. Women without cervical cancer aged 23–32 and 43–59 years at recruitment and residing in all three regions increased their use of GPs from the before to the after period, while this was not the case for women aged 33–42 years; probably reflecting a decrease in contacts related to pregnancy. Although an increase in number of GP contacts was observed also for women with cervical cancer and residing in the Capital and Islands, the increase was larger in women with than in women without cervical cancer only in women aged 43–59 years and in women living in Jutland.

#### 3.2. Contacts to hospitals

Contacts to hospitals were far less frequent than contacts to GPs. In the “before” period, 53% of women later diagnosed with cervical cancer had no hospital contacts. In the “after” period this was only 10%. In women without cancer, 69% had no hospital contacts in the “before” period and this was unchanged in the “after” period with 68% (Table 2). For women with cervical cancer this was reflected in a mean number of 0.98 contacts to hospitals in the “before” period and 5.17 in the “after” period, thus an increase of 4.18 contacts (95% CI: 4.06–4.31) (Fig. 2). For women without cervical cancer the mean numbers were 0.63, 0.69 and 0.06 (95% CI: 0.056–0.064), respectively. Contacts to hospitals were increased with 4.12 (95% CI: 3.99–4.25) more contacts in women with cancer than in women without. This pattern was seen in all age-groups and regions.

#### 3.3. Contacts to psychologists/psychiatrists

The majority of women (93%) in both groups had no contact with a psychologist and/or psychiatrist in the “before” period, and the same was true in the “after” period (86% and 91% for women with and without cancer, respectively) (Table 2). For women with cervical cancer the mean number of contacts to psychologists/psychiatrists increased with 0.90 (95% CI: 0.43–1.37) from the “before” to the “after” period (Fig. 3), and for women without cervical cancer with 0.40 contacts (95% CI: 0.38–0.41), thus basically the same in the two groups with a difference in increase of 0.50 contacts (95% CI: 0.03–0.97). The same tendency was observed across age-groups and regions.

#### 3.4. Use of prescription drugs

In women with cervical cancer, the proportion using analgesic prescription drugs increased from 22% in the “before” period to 39% in the “after” period. In women without cervical cancer, also 22% used analgesic drugs in the “before” period, and this use increased to 27% in the “after” period. The increase was 80 DDD (95% CI: 60–100) higher in women with than without. Regarding use of psychotropic prescription drugs, the proportions were 29% and 43%, respectively, for women with cervical cancer; and 28% and 35%, respectively, for women without (Table 2) with 304 DDD (95% CI: 261–347) more in women with cancer than without. In women with cancer, total use of prescription drugs increased with a mean of 539 DDD (95% CI: 489–587) over the 10 years, as compared with 154 DDD (95% CI: 153–156) in women without cervical cancer with a difference between the two groups of 385 DDD (95% CI: 336–434) (Fig. 4). As seen in Fig. 4, the contributions to the development of a difference between women with and without cervical cancer came from women aged 33–42 and 43–59 years and coming from the Islands and Jutland, while no significant difference was observed over time between women with and without cervical cancer in the younger age 23–32 years and coming from the Capital.

### 4. Discussion

To our knowledge this is the first population-based register study to address the potential impact of a cervical cancer diagnosis on the use of health care. There were two important findings from this population-based register study. First, we observed that a diagnosis of cervical cancer was followed by an increase in the use of GPs, hospitals and prescribed analgesic- and psychotropic drugs from the five years before the diagnosis to the five years after, while the use of psychologists/psychiatrists was not affected. Second, aging and/or calendar time affected health care and drug use, underlining the importance of using a comparison group of women without cervical cancer in the analysis of changes over time. These findings will be discussed below.

In Denmark, the GPs are the gatekeepers to the health care system either treating the patients themselves or referring them for further diagnostics and treatment. This was reflected in the comparatively large number of contacts for all women in the “before” period with almost one contact per month to the GP for each woman. The difference in number of contacts to the GP from “before” to “after” increased with a mean of three contacts per year for a woman with cancer and one contact per year for women without cancer. This larger increase for women with cervical cancer was expected, as almost all of these women had undergone surgery and may contact their GP regarding short-term inconveniences, e.g. bleeding, pain, renewal of analgesic prescription drugs, or permanent consequences following operation and/or radio- and chemotherapy such as pain, urinary- and bowel discomfort or problems
with sexual functioning [2]. Of notice, the higher increase in number of GP contacts was primarily observed in the oldest age group and mainly in women living in Jutland. We may speculate that treatment related complications and late effects may have a greater impact on the life of the elderly women and that demographics and culture is likely to influence on the use of GP visits.

The women who were later diagnosed with cervical cancer already differed in the use of hospital contacts compared with women without cancer in the five years “before” the diagnosis. The cervical cancer diagnosis further increased this difference; adding nearly an extra hospital contact per year, while only a minor change was seen in women without cervical cancer. In our study, the index operation was excluded from the analysis. Nevertheless, to determine the FIGO stage of the cervical cancer patients, women were offered gynecological examination in general anesthesia and more biopsies could be taken. According to the guidelines at the time of patient recruitment, cystoscopy and proctoscopy were performed to determine potential spread to the bladder and rectum, respectively [13]. Further diagnostics could also be performed such as x-rays and MRI. Diagnostic imaging and clinical staging procedure are hence most often performed at the hospitals. Postoperative follow-ups are either performed at the department of gynecology or oncology. In conclusion, normal pre- and postoperative procedures and investigations are likely to account for the increased pre-diagnostic or post-diagnostic use of GPs and hospitals for women with cervical cancer compared with women without cancer. Notably, one in ten women with cervical cancer still did not have any contact to the hospital after the cancer diagnosis. This might reflect that in Denmark, in the period relevant for our patient population, 17.0% of the cervical cancer cases had stage IA1 disease [15] and most likely underwent conization only. Another explanation may be that women were non-adherent to follow-up. Our data were not able to uncover this.

In 2017, treatment guidelines were changed and became more conservative recommending conization to be considered in stage IA1 and IA2 with or without vascular invasion [21]. Furthermore, between 2008 and 2015, robotic minimally invasive surgery was introduced for the treatment of early stage cervical cancer [22]. These changes may lower the post-diagnostic use of GPs and hospitals, as the treatment is gentler and side effects and permanent consequences are expected to be fewer. Minimally invasive surgery might, however, lead to increased recurrence, as seen in the Laparoscopic Approach to Cervical Cancer Trial (LACC) [23]. However, in a Danish population-based observational study, that was launched after the release of the preliminary LACC results, it was demonstrated that implementation of robotic minimally invasive surgery for early-stage cervical cancer in Denmark was not associated with increased risk of recurrence or death [22]. Change in surgical modality is therefore not likely to generate an increase in health care utilization.

In contrast, all women had limited use of psychologists and/or psychiatrists, and the cervical cancer diagnosis did not affect this pattern. These findings were somewhat surprising. In Denmark, there is access to a psychologist/psychiatrist after a referral from the GP with a cost discount of 60% for up to 12 consultations based on indications as suffering from a serious invalidating disease, mild/ moderate depression as well as other indications [24]. The limited use of psychologist/psychiatrist after a diagnosis of cervical cancer may have several explanations. First, women may find it difficult to afford even with the price discount. Second, the GPs and hospitals may provide sufficient psychological support during the follow-up visits to the hospital as described earlier [21]. Third, there are well-functioning Danish patient associations, as the Danish Cancer Society [25], where patients can seek support with other women sharing the same survivorship issues as themselves. This may lower the need for psychologist/psychiatrist treatment [25]. However, our findings may also reflect a general lack of attention to psychological consequences of cervical cancer patients.

Studies have demonstrated that mental health is lower in cervical cancer survivors especially compared with age-matched women from the general population without cancer [2,4]. One study found that 15-year survivors had a lower emotional functioning, decreased global health status, and more mental fatigue than five- and ten-year survivors [5]. It was hypothesized that either treatment had improved over time resulting in fewer permanent consequences or that permanent consequences might worsen over time [5]. In our study, we estimated health consequences might worsen over time [5]. In our study, we estimated health care use within five years after the cervical cancer diagnosis. If we had used a longer follow-up period, we might have observed an increase

Table 2
Distribution of study population by use of health care resources.

<table>
<thead>
<tr>
<th>Contacts to GP:</th>
<th>Women with cervical cancer</th>
<th>Women without cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before (%)</td>
<td>After (%)</td>
</tr>
<tr>
<td>0-23</td>
<td>267(29)</td>
<td>232(25)</td>
</tr>
<tr>
<td>24-53</td>
<td>310(33)</td>
<td>304(33)</td>
</tr>
<tr>
<td>54-79</td>
<td>176(19)</td>
<td>147(16)</td>
</tr>
<tr>
<td>80+</td>
<td>173(19)</td>
<td>243(26)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contacts to hospital:</th>
<th>Women with cervical cancer</th>
<th>Women without cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>488(53)</td>
<td>91(10)</td>
</tr>
<tr>
<td>1</td>
<td>233(25)</td>
<td>178(19)</td>
</tr>
<tr>
<td>2</td>
<td>114(12)</td>
<td>146(16)</td>
</tr>
<tr>
<td>3+</td>
<td>90(10)</td>
<td>511(55)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contacts to psychologist/psychiatrist:</th>
<th>Women with cervical cancer</th>
<th>Women without cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>858(93)</td>
<td>796(86)</td>
</tr>
<tr>
<td>1-4</td>
<td>24(2)</td>
<td>40(4)</td>
</tr>
<tr>
<td>5-9</td>
<td>19(2)</td>
<td>38(4)</td>
</tr>
<tr>
<td>10+</td>
<td>25(3)</td>
<td>52(6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Analgesic prescription drugs, DDD:</th>
<th>Women with cervical cancer</th>
<th>Women without cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>720(78)</td>
<td>564(61)</td>
</tr>
<tr>
<td>1-59</td>
<td>158(17)</td>
<td>210(23)</td>
</tr>
<tr>
<td>60-259</td>
<td>27(3)</td>
<td>73(8)</td>
</tr>
<tr>
<td>260+</td>
<td>21(2)</td>
<td>79(8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychotropic prescription drugs, DDD:</th>
<th>Women with cervical cancer</th>
<th>Women without cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>661(71)</td>
<td>526(57)</td>
</tr>
<tr>
<td>1-59</td>
<td>124(13)</td>
<td>137(15)</td>
</tr>
<tr>
<td>60-259</td>
<td>44(5)</td>
<td>70(7)</td>
</tr>
<tr>
<td>260+</td>
<td>97(11)</td>
<td>193(21)</td>
</tr>
</tbody>
</table>
### Fig. 1
Mean number of contacts to GP by period (before/after) and exposure (with/without) and stratification by age and region. Mean of differences in number of contacts to GP from “after” minus “before” period by exposure, and difference-in-differences (diff-in-diff) between exposure groups.

<table>
<thead>
<tr>
<th>Contact to GP</th>
<th>Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with cancer:</td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>52.4 (48.1-56.7)</td>
</tr>
<tr>
<td>After</td>
<td>66.5 (62.1-70.8)</td>
</tr>
<tr>
<td>Difference</td>
<td>14.1 (10.3-17.8)</td>
</tr>
<tr>
<td>Women without cancer:</td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>55.2 (52.0-58.3)</td>
</tr>
<tr>
<td>After</td>
<td>60.6 (56.5-60.7)</td>
</tr>
<tr>
<td>Difference</td>
<td>5.5 (5.3-5.6)</td>
</tr>
<tr>
<td>Diff-in-diff</td>
<td>8.6 (4.8-12.4)</td>
</tr>
</tbody>
</table>

### Fig. 2
Mean number of contacts to hospital by period (before/after) and exposure (with/without) and stratification by age and region. Mean of differences in number of admissions to hospital from “after” minus “before” period by exposure, and difference-in-differences (diff-in-diff) between exposure groups.

<table>
<thead>
<tr>
<th>Contact to hospital</th>
<th>Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with cancer:</td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>0.98 (0.88-1.09)</td>
</tr>
<tr>
<td>After</td>
<td>5.17 (5.06-5.27)</td>
</tr>
<tr>
<td>Difference</td>
<td>4.18 (4.06-4.31)</td>
</tr>
<tr>
<td>Women without cancer:</td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>0.63 (0.627-0.633)</td>
</tr>
<tr>
<td>After</td>
<td>0.69 (0.687-0.693)</td>
</tr>
<tr>
<td>Difference</td>
<td>0.06 (0.056-0.064)</td>
</tr>
</tbody>
</table>
in psychologists/psychiatrists because as indicated by previous studies, there might be a delay for psychological consequences to manifest. Women who underwent radiotherapy had lower mental health compared with other cervical cancer survivors [4,5]. Also, women diagnosed and treated for cervical cancer during their reproductive age experienced psychological survivorship sequelae and reproductive concerns and it seemed to persist five to ten years post-diagnosis [3]. This could indicate that these groups of women constitute more vulnerable groups of women who require special attention in the post-diagnostic years. Sexual health in cervical cancer survivors has also been a concern in recent years and one study found that more than half of cervical cancer survivors had sexual health concerns [26]. As women with the health concerns uncovered in the quoted studies may benefit from psychologist/psychiatrist treatment, a higher referral rate of cervical cancer patients may be beneficial.

Women diagnosed with cervical cancer increased their intake of analgesic- and psychotropic prescription drugs more than three times from before to after the diagnosis, while the use only nearly doubled over the same period in women without cancer. During the five years after the diagnosis of cervical cancer the women consumed on average one DDD of these prescription drugs every 2–3 days. The increased use of analgesic was expected as it is a natural part of the post-operative treatment. The increased use of psychotropic prescription drugs was less expected though supporting the findings of the studies described above documenting mental health concerns in cervical cancer survivors [2–5].

Nevertheless, also women without cervical cancer increased their use of analgesic- and psychotropic prescription drugs. In the five years after their index screening date, on which far the majority had a normal cytology, their average use was one DDD every fifth day. The increase was seen in all age-groups and in all regions. This development could be related to the aging over the study period and/or to the change in calendar time from before to after the index date.

The seemingly universal and permanent use of analgesic and psychotropic drugs in Danish women with cervical cancer but also in women without cancer seems alarming. We observed that women without cervical cancer on average had a long-term use of these drugs of one DDD every fifth day, and that women after a diagnosis of cervical cancer had on average the double long-term use.

In Denmark, a subsidy is granted for prescribed drugs lowering the costs for the patients. The government pays prescribed drugs partly when a patients' costs exceed 135 euro per year, and all expenses are held by the government after a self-payment of 665 euro per year [27]. However, long-term use of some analgesic/psychotropic prescription drugs e.g. benzodiazepines are known to be associated with adverse effects such as dependence, tolerability, misuse, and withdrawal symptoms [28,29]. Attention has therefore been given to limiting the intake of these drugs [28].

Given the cervical cancer patients' low level of contacts to psychologists/psychiatrists, replacement of part of the drug use with psychological support might be an option to consider. In 2010, a year included in the studied data, Denmark was number two on the OECD-list over countries consuming most antidepressants, but by 2017 Denmark had moved to the number seven position on the list [30]. Also, Danish prescriptions of benzodiazepine decreased from 2003 to 2013 with a 66% reduction in prescriptions of long-acting benzodiazepine [31]. In conclusion, the ambition in Denmark of lowering the use of certain prescription drugs seems to have succeeded.

The primary strength of this study was the comprehensive study population including the entire Danish population, which minimized the risk of selection bias. The use of register data was also a strength eliminating the risk of recall bias. The availability of the unique personal identification numbers allowed linkage of data for each woman individually and secured almost no loss to follow-up. Women undergoing screening were considered to represent the most appropriate comparison group. Nevertheless, using all women as the comparison group would probably not have affected the results, as a previous study found that 90% of women undergo cervical cancer screening at least once in an 8-year period [32]. A limitation may be that there are some baseline differences between women with a diagnosis of cervical cancer and women undergoing screening without cervical cancer. This may
have introduced selection bias and we were not able to take this into account.

To ascertain data on health care use for a five-year period after the diagnosis of cancer, we had to exclude women who died during these five years. Therefore, the group of women with cervical cancer is a slightly selected group; but in the recruitment period the 5-year survival rate of patients in the studied age-group was 83% [33,34]. The excluded women probably had a higher number of hospital contacts resulting in an underestimation of health care use for women with cervix cancer. From the registers, we were not able to include patient-related outcome measurement data, which would have provided valuable information on perceived health status.

5. Conclusion

A diagnosis of cervical cancer increases the woman’s use of GPs, hospitals and intake of prescription drugs but did not increase the use of psychologist/psychiatrist, indicating that pain and mental health concerns following the diagnosis either persisted or may have been alleviated by other means e.g. additional contacts to the health care system, to patient organizations, and/or pharmacologically. In the five years following the diagnosis, the patients used on average one DDD of analgesic/psychotropic prescription drugs every 2–3 days, which was the double of the use in women without a diagnosis of cervical cancer. Considering the amount used of these drugs in cervical cancer survivors, one might speculate if a higher referral rate to psychologist/psychiatrist could lower the use of these drugs and hence avoid potential, unwanted side effects.

Author contributions

MS: Writing – original draft preparation. MEF: Data curation, Writing – original draft preparation. MV-PB: Methodology, Formal analysis, Writing – reviewing and editing. A-BB: Formal analysis. PTJ, JH: Writing
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Declaration of Competing Interest

MS, MF, MVPB, AB, PTJ, JH and CR declare no potential conflicts of interest. EL receives test kit from Roche for a method study.

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