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Identification of Ovarian Cancer Symptoms in Health Insurance Claims Data

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Abstract

Background: Women with ovarian cancer have reported abdominal/pelvic pain, bloating, difficulty eating or feeling full quickly, and urinary frequency/urgency prior to diagnosis. We explored these findings in a general population using a dataset of insured women aged 40–64 and investigated the potential effectiveness of a routine review of claims data as a prescreen to identify women at high risk for ovarian cancer.

Methods: Data from a large Washington State health insurer were merged with the Seattle-Puget Sound Surveillance, Epidemiology and End Results (SEER) cancer registry for 2000–2004. We estimated the prevalence of symptoms in the 36 months prior to diagnosis for early and late-stage ovarian cancer cases and for two comparison groups. The potential performance of a passive screener that would flag women with two or more visits for any of the symptoms in the previous 2-month period was examined.

Results: Of the 223,903 insured women, 161 had incident cases of ovarian cancer. Both early and late-stage patients had a higher prevalence of abdominal/pelvic pain and bloating than the comparison groups, primarily in the 3 months before diagnosis. The passive screener had a sensitivity of 0.31 and specificity of 0.83 and usually identified women right before diagnosis. Assuming an average cost of $500 per false positive, the screener would be considered cost-effective if the true positives had an average increase of 8.5 years of life expectancy.

Conclusions: These results support previous findings that ovarian cancer symptoms were reported in health insurance claims and were more prevalent before diagnosis, but the symptoms may occur too close to the diagnosis date to provide useful diagnostic information. The passive screening approach should be reevaluated in the future using electronic medical records; if found to be effective, the method may be potentially useful for other incident diseases.

Introduction

Ovarian cancer has the seventh highest incidence of all cancer among women in the United States.1 The majority (67%) of cases are diagnosed at a distant stage, where 5-year survival is estimated to be 30%. However, when the disease is confined to the ovary, survival rates are approximately 70%–90%.2 With this clear difference in survival based on the stage of diagnosis, studies have explored potential symptoms of the disease that could lead to earlier detection. Recent research has shown that four key symptoms—bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, and urinary urgency and frequency—are reported frequently in women with ovarian cancer at both early and late stages of disease.3–6

Several studies have used either private insurance or Medicare claims data to investigate healthcare use prior to ovarian cancer diagnosis. These studies highlighted that women with ovarian cancer tend to have claims related to these four key symptoms more often than controls, particularly in the 3–6 months before diagnosis.7,8 Goff et al.9 have suggested that these symptoms could be used to screen for ovarian cancer. Using prospective case-control data among women about to undergo a pelvic/abdominal ultrasound examination, they developed a screening index that was considered positive if a woman had...
12 or more occurrences of any of the three key symptoms (excluding urinary) per month in the last year. In confirmatory data, the index provided a sensitivity of 56.7% and 79.5%, for early and late-stage cancer, respectively, and a specificity around 90%. Additional studies have examined the combined predictive power of a symptom index with CA 125.

In addition to symptom-based screening methods, two recent randomized trials have compared the use of CA 125 or transvaginal ultrasound or both as annual screening modes to identify incident ovarian cancer in postmenopausal women aged 50–74. The first trial provided a sensitivity and specificity for all primary ovarian and tubal cancers of 89.4% and 99.8%, respectively, using CA 125 as an annual screen with transvaginal ultrasound as a second line, and 84.9% and 98.2%, respectively, using transvaginal ultrasound alone as an annual screen. Preliminary results from the second randomized trial estimated that the positive predictive value (PPV) ranged from 2.1% to 3.2% for CA 125 and from 0.7%–1.1% for transvaginal ultrasound. Although these studies did not address cost-effectiveness, current theoretical research has further identified situations in which screening for ovarian cancer would be cost-effective and reduce mortality.

In the current study, we aimed first to confirm previous findings about the presence of the four highlighted symptoms in a general insured population and to evaluate whether these symptoms can be used as a prescreener to identify women at high risk for ovarian cancer. We used the Surveillance, Epidemiology, and End Results (SEER) data to identify the cases and ICD-9 codes in the insurance data to identify symptoms. We compared the trends of symptoms preceding ovarian cancer diagnosis with trends for women diagnosed with breast cancer and with the general insured population. As Washington state requires that services provided by licensed complementary and alternative medicine (CAM) practitioners be included in private health insurance benefits, we were able to include claims from both conventional and CAM providers. We stratified this analysis based on the stage of ovarian cancer to determine if any excess in claims related to the four symptoms was predominantly for women with late-stage cancer. Second, we explored whether claims data might be used to improve the early detection of ovarian cancer by identifying women who may be at high risk for ovarian cancer. We estimated the number of true and false positive results of a hypothetical screening rule and determined the circumstances under which this screening would be cost-effective.

Materials and Methods

Population

This study was approved by the Institutional Review Boards of the University of Washington and Fred Hutchinson Cancer Research Center. Study participants consisted of women 40–64 years of age who lived in the 13 county region served by the Seattle-Puget Sound SEER cancer registry and were enrolled in a comprehensive insurance plan offered by the participating insurance company. Products provided by the insurer included health maintenance organization (HMO), point of service (POS), preferred provider organization (PPO), or traditional indemnity insurance (TRD) plans. Federal employees and their dependents were not included, as were enrollees in publicly funded plans.

Data collection

The researchers received separate insurance files with enrollment and medical utilization (claims) data for 2000 through 2004. The techniques used to process these data and define study variables have been described previously. Participants with incident ovarian cancer were identified through a confidential link of the insurance data with the SEER cancer registry. The linking process has been described previously. At the time of the link, SEER maintained diagnosis data from 1974 though 2006 and provided the calendar month of diagnosis and the cancer stage at diagnosis. Because SEER has been estimated to identify 97.7% of cancer diagnoses, we expect to capture the majority of ovarian cancer cases in our defined population.

A consensus by the Gynecologic Cancer Foundation (GCF), Society of Gynecologic Oncologists, and American Cancer Society highlighted four major symptoms of interest: (1) pelvic or abdominal pain, (2) difficulty eating or feeling full quickly, (3) bloating, and (4) urinary symptoms (urgency or frequency). Patient visits to both conventional care providers (physicians, advanced registered nurse practitioners, and physician’s assistants) and CAM providers (chiropractors, naturopathic physicians, licensed massage therapists, and acupuncturists) were classified as to the presence of these symptoms based on International Classification of Disease (ICD-9) codes, as shown in the Appendix.

Early-stage incident ovarian cancer was defined as the American Joint Committee on Cancer’s stages IA, IB, and IC (T1a, N0, M0; T1b, N0, M0; and T1c, N0, M0, respectively). In stages IA, IB, and IC, the cancer is still confined to the ovary (or ovaries) without involvement of the nodes or metastases to other structures. The late stage was defined as stage II or higher.

Statistical analysis

As a descriptive measure, we calculated the incidence rate of ovarian cancer in our study population by age and insurance characteristics. Person-years at risk were calculated from the number of months with insurance coverage, with covered months after an incident ovarian diagnosis excluded. Incident cases were defined as cancers diagnosed while a woman had coverage because coverage is required for the person-years at risk calculation. Other analyses either relaxed this condition or required 12 months of continuous coverage prior to diagnosis. Figure 1 lists the coverage restriction for each statistical analyses.

Women diagnosed with ovarian cancer prior to 2000 or women who had undergone an oophorectomy were not removed from the calculation of person-years at risk. Therefore, our calculated incidence rates may not be a proper estimate of the true rate in the population of at-risk women aged 40–64. The estimates are provided to compare relative rates across groups of interest.

Identification of symptoms

Each incident ovarian cancer case, as defined above, was matched to two incident breast cancer cases and also to two women in the general insured population who were not in SEER (cancer free). Women in the cancer-free cohort were assigned a pseudodiagnosis date, chosen as the date of a
randomly selected medical claim within their respective coverage window. The matches were within ± 2 months of diagnosis and ± 2 years of age of each case.

Initially, we calculated the proportion of women who had at least one medical claim related to each of the four symptoms, separately, in the 1–12 months prior to diagnosis. Women were required to have uninterrupted insurance coverage from 12 months before diagnosis up to the month of diagnosis. For each symptom, we descriptively compared the proportion of women who had a claim reporting the symptom in either the breast cancer or general control group with the proportion of women in the ovarian cancer group, using a t test.

Second, in a more flexible and descriptive approach, we calculated the proportion of women, among those with insurance coverage for that month, who had at least one symptom-related claim in that month. This calculation was done separately for each of the 36 months preceding diagnosis, and the number of eligible women varied by month. No insurance coverage restrictions were placed on the cases or matched controls outside of having coverage during the month of diagnosis. Coverage during the month of diagnosis was required because a random insurance claim was used as diagnosis date for the cancer-free controls. Women diagnosed within 36 months from the start of the study were included for the months available between the time of diagnosis and the beginning of an individual’s coverage period. We used a smoothing spline to show the proportion with a related claim across the months prior to diagnosis for early and late-stage ovarian cancers and the two control groups.

**Evaluating a claims-based screening rule**

Modifying the prior symptom index definitions for use as a screening tool for insurance claims, we evaluated a hypothetical routine screening program in which the insurer’s computer program would flag any woman with two or more claims in the previous 2 months for any of the four symptoms. The woman’s provider would presumably be notified of any positive screen, and the provider would attempt to rule out cancer through some combination of history, CA 125, transvaginal ultrasound, or surgery. We evaluated this hypothetical program as follows. Starting with the initial 2 months of the available data—January and February of 2000—we determined how many women had a positive screen (two or more visits with these symptoms). We considered the screen a true positive (TP) if the woman had an incident SEER-defined ovarian cancer diagnosis in the following 12 months. For this phase of the study, women were not required to have insurance coverage for this entire period or at the time of diagnosis because the insurance company would not have access to that future information at the time of screening.

Women with a positive symptom screen, but without an incident diagnosis in the subsequent 12 months, were considered one of two types of false positives (FP). One group, “no cancer,” had a positive screen but remained free of an incident ovarian cancer through December 2005. The second group, “eventual cancer,” had a positive screen and a diagnosis of ovarian cancer more than 12 months after the months in review but prior to December 2005. We then repeated the process of determining a positive screen using claims from February and March of 2000 and so on until November and December of 2004. Once a woman screened positive, she was removed from consideration for the subsequent months. Among TP women, we descriptively examined the number of months between the positive screen and the date of the ovarian cancer diagnosis.

**Cost-effectiveness of a passive screener**

Cost-effectiveness analyses are usually based on the incremental cost-effectiveness ratio (ICER). The numerator of
the ratio is the incremental cost, which is the average additional cost for the FP multiplied by the number of FPs. Unlike most screening methods, the true negatives here add no additional cost to the program, as their claims are reviewed by an automated computer program. Any costs associated with the TPs are also not included in the ICER calculation, as these costs would occur regardless of any screening program. The denominator is the mean benefit, measured in mean incremental (quality-adjusted) years of life saved (YLS) among the TPs. The ICER is then defined as:

$$\text{ICER} = \frac{\text{FP} \times \text{cost}}{\text{TP} \times \text{YLS}}$$

The numbers of TPs and FPs are known after applying the screening rule. The incremental costs would include both financial and nonmonetary costs. The financial costs of actually identifying the women would be negligible because it would involve only a monthly computerized review of claims data. Therefore, the incremental cost would be the costs of following up the FPs. These costs would include such things as the cost of notifying the providers and the costs of ruling out cancer by the strategy chosen by the provider. Some women will require no additional medical follow-up after a physician reviews her history, acquiring further details on the types, frequency, and duration of symptoms. At this point, women who have had a previous ovariectomy will also be identified. Other women might require additional medical procedures, such as CA 125 or transvaginal ultrasound screening, and positive results on those tests might require laparoscopy or other surgery. In King County, Washington, in 2009, Medicare reimbursed $192 for an office visit, blood draw, CA 125 determination, and also performing a transvaginal ultrasound. For this example, we considered two possible values for this average cost of FPs (including those who needed no additional medical follow-up), $200 and $500. The nonmonetary costs of a screening program include time costs, anxiety, and unnecessary surgery for the FPs. These costs unfortunately cannot be addressed further in this preliminary study.

Because we had little information about the YLS by earlier detection of ovarian cancer, we solved for the YLS value that would make the screener cost-effective instead of estimating the ICER. An ICER of $50,000 per additional year of life is traditionally considered to be at the threshold for cost-effectiveness, and at an average cost of $500 per FP, the screener would achieve this threshold if:

$$\text{YLS} > (\text{FP} \times \$500)(\text{TP} \times \$50,000)$$

We also determined the average YLS that would be needed if the average cost for each FP were $200.

All analyses were conducted using the R statistical package. No adjustments were made for multiple comparisons.

Results

There were 225,903 women included in the analysis. Descriptive statistics for the sample are provided in Table 1. The average age was 50.3 years, and the sample was split relatively evenly between the 40–49 and 50–64 age groups. Most women were enrolled in a PPO (49%) or POS product (39.7%) and were covered by a group policy (87.2%). Only 23.7% of study subjects had a policy where the insurance company did not assume the financial liability but rather was contracted just to provide administrative services.

There were 161 women identified with ovarian cancer in the period. Figure 1 shows which cancer cases were used in each analysis. The incidence rate of ovarian cancer was 17.9/100,000 person-years. Incidence rates were higher in the older age category compared with the younger (24.5 and 11.3, respectively). The rate of cancer was similar among the different insurance products, except for traditional, where the rate appeared lower.

Identification of symptoms

Of the 82 women diagnosed with ovarian cancer who had a full 12 months of insurance coverage before diagnosis, a total of 42 (51%) had at least one claim related to abdominal or pelvic pain in the previous 12 months (Table 2). This proportion (0.51) exceeds the proportion in the breast cancer or general control group that had a related claim (0.14 and 0.12, respectively). A claim related to bloating was also more likely in the 12 months before diagnosis for women with ovarian cancer compared with the two control categories, where it was very infrequent. There were modest differences for claims related to urinary urgency or frequency and difficulty eating or feeling full quickly. Among the women with a symptom-related claim, only two women ever saw a CAM provider for the associated symptom. Almost all the related claims (99%) were from conventional care providers.

Figure 2 presents the (smoothed) proportion of women with each symptom in the 36 months before diagnosis, with the rightmost value representing the month before diagnosis. The proportions were similar across the groups from 36 to...
around 3 months before diagnosis. At that point, there was a sharp increase in claims related to abdominal or pelvic pain and bloating in the two ovarian cancer groups. There was no increase in difficulty eating or feeling full or in urinary urgency or frequency. Although both ovarian cancer groups had an increase in abdominal or pelvic pain, the proportion was higher among the late-stage cancers. There was no evidence of a stage-related difference in bloating.

Evaluating a claims-based screening rule

Table 3 presents the results of the passive screen for two or more symptoms reported in the prior 2 months. There were 161 new ovarian cancer diagnoses in 225,903 total women, all of whom were included in this analysis. A total of 38,421 women had a positive screen (two or more symptoms in 2 months), and 45 of these women were diagnosed with ovarian cancer in the subsequent 12 months (TP). An additional 17 women were diagnosed with ovarian cancer but more than 12 months after the positive screen (FP, eventual cancer). There were 38,359 women with a positive screen who remained free of incident ovarian cancer 12 months after the study window (FP, no cancer). Of the FP, no cancer women, 1,247 (3.2%) had a positive screen from at least one CAM visit. None of the TP or FP, eventual cancer, women fulfilled the screening rule with a CAM-related visit. Combining the two types of FPs, the sensitivity of the test was 0.31, and the specificity was 0.83. The positive predictive value of the test was 0.0012. Among the 45 TP women, the majority (69%) were diagnosed with late-stage cancer. This proportion was greater for FP, eventual cancer, women (88%) and for those women who never satisfied the screening rule but were diagnosed with cancer (85%).

We further calculated the number of months between the positive screen and the month of SEER diagnosis for the 45 TPs (Fig. 3). The majority of TPs (58%) fulfilled the screen criteria in the month just prior to diagnosis.

Cost-effectiveness of a passive screener

With 45 TPs, 38,376 FPs, and an assumed average incremental cost of $500, the program would be considered cost-effective (ICER of $50,000 per year) if the average life expectancy of the 45 TPs were to increase by 8.5 years because of screening. Under this situation, the incremental cost-effectiveness ratio is:

\[
\text{ICER} = \frac{\text{FP} \times \text{cost}}{\text{TP} \times \text{YLS}} = \frac{38,376 \times 8500}{45 \times 8.5} = \frac{50,000}{\text{year}}
\]

If the incremental cost were instead $200, the average YLS would need to be 3.4 years.

Discussion

We found that the four symptoms highlighted by GCF were reported on claims data and that the prevalence of two of them, abdominal or pelvic pain and bloating, increased sharply shortly before a diagnosis of ovarian cancer. Symptom prevalence was relatively infrequent and flat for women diagnosed with breast cancer and women in the general cancer-free population. The abdominal or pelvic pain and bloating results support the findings of previous studies in a different insured population.7,8 The prevalence of claims related to urinary urgency or frequency and difficulty eating or feeling full did not increase before diagnosis. Adding to the published literature, we found no evidence that the four symptoms were exclusively associated with late-stage ovarian cancer. The proportion with a claim related to difficulty eating or feeling full quickly, bloating, and urinary urgency or frequency appeared similar for early and late-stage ovarian cancers. A greater proportion of women with late-stage cancer had a claim related to abdominal or pelvic pain compared with women with early-stage disease in the 3 months preceding diagnosis.

Using the defined passive screen of two or more symptomatic visits in a 2-month window, we identified 45 of the 161 ovarian cancers cases and incorrectly classified 38,376 women. These results produced a sensitivity and specificity of 0.31 and 0.83, respectively, and a PPV of 0.0012.

Although the estimated PPV is well below the minimum 0.10 PPV threshold used by epidemiologists in evaluating screening programs,22 the passive screening method presented here differs from other screening programs. Traditional screens for ovarian cancer propose a particular procedure, such CA 125 or transvaginal ultrasound, to be performed on an entire subpopulation of women. The large number of true negatives, all of whom have undergone the screening procedure, makes these screening approaches very expensive. Our screening method differs, as it is attempting to identify women who may be at high risk for ovarian cancer based on their previous symptoms. In this sense, this method could be considered a prescreen, as it is identifying women who may benefit from a traditional screening program. Because the actual screening process involves only a computerized review of claims, there are little, if any, costs associated with the true negatives.

Among the 45 women correctly identified, the majority fulfilled the screen criteria 1 or 2 months before their diagnosis. This short period of time suggests that the screen may simply be capturing part of the diagnostic process. These
women may have shared the symptoms with their healthcare provider, and the conditions were recorded in the claims when the physician referred the patient for appropriate diagnostic testing. If so, screening by the insurer probably would not have led to earlier diagnosis for these women. This situation would affect our cost-effectiveness analysis. We assumed these women were not yet involved in the diagnostic process and, further, that being diagnosed 1 or 2 months earlier could have some impact on life expectancy. We could attempt to avoid this assumption by removing the 33 women whose positive screen occurred within 2 months of diagnosis. In this situation, the remaining 12 TPs would need to gain an average of 32 additional years of life to make the intervention cost-effective. This situation would be unlikely, given the high percentage diagnosed at a late stage and the low associated 5-year survival probability.

Prevalent ovarian cases (those diagnosed prior to January 2000) and women who underwent previous oophorectomies were not identified or removed from the analytic data. Published statistics estimate that by age 60, over one third of U.S. women have undergone hysterectomy, and approximately half of those concurrently had an oophorectomy. If one sixth of the FPs could be ruled out on this basis, the incremental

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**Table 3. Results from Passive Screen of Claims over 60-Month Study Window**

<table>
<thead>
<tr>
<th>Total</th>
<th>Proportion late stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of women included</td>
<td>225,903</td>
</tr>
<tr>
<td>Incident ovarian cases&lt;sup&gt;a&lt;/sup&gt;</td>
<td>161</td>
</tr>
<tr>
<td>Screening results</td>
<td></td>
</tr>
<tr>
<td>True positive</td>
<td>45</td>
</tr>
<tr>
<td>False positive, no cancer&lt;sup&gt;b&lt;/sup&gt;</td>
<td>38,359</td>
</tr>
<tr>
<td>False positive, eventual cancer&lt;sup&gt;c&lt;/sup&gt;</td>
<td>17</td>
</tr>
<tr>
<td>False negatives</td>
<td>99</td>
</tr>
<tr>
<td>True negatives</td>
<td>187,383</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.83</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.31</td>
</tr>
<tr>
<td>Positive predictive value (PPV)</td>
<td>0.0012</td>
</tr>
<tr>
<td>Negative predictive value (NPV)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

<sup>a</sup>Includes cases diagnosed up to 12 months after a woman’s last month of coverage.
<sup>b</sup>No cancer are women with a positive screen who did not have incident cancer in the study window or thereafter.
<sup>c</sup>Eventual cancer are women with a positive screen who had incident cancer more than 12 months after screen.

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**FIG. 2.** Smoothing spline of the proportion of women with a visit related to each of the four highlighted symptoms in the 1–36 months prior to diagnosis. The month of diagnosis was not included; (—) ovarian, early stage; (– – –) ovarian, late stage; (- - - - -) breast; (— • — • —) cancer free.
costs might be lower and the screening program more cost-effective.

These results are the product of only one of many potential screening rules. Of the ovarian patients, 137 reported one or more of the symptoms at some point before diagnosis. An optimized screening rule could have a sensitivity no higher than 137/161 = 0.85. Alternative rules could vary the length of the analysis window and the number or variety of symptoms required. Based on the Figures 2 and 3, changing the time window would provide little benefit; these symptoms are most common right before diagnosis. Varying the number and type of symptoms to be more inclusive could potentially increase the FP rate.

The general performance of this screening rule, as with any potential screen for ovarian cancer, is limited by the rarity of the cancer. The lifetime risk of invasive ovarian cancer is estimated to be 1.4% in the United States; therefore, screening programs will inevitably identify many healthy women who may undergo unnecessary surgeries. These unnecessary surgeries will inflate the cost of any screening method.

Washington state’s requirement that insurers provide coverage of CAM did not appear to impact our results. Very few women had a CAM provider claim related to any of the highlighted symptoms. Therefore, our results should generalize to states without mandatory CAM coverage.

Limitations

There are several limitations to the study. The use of insurance claims to capture the key ailments shared between participants and their healthcare providers could be problematic. If the provider had not attributed the symptoms to a diagnosable condition, the individual’s symptoms may not have been present on the insurance billing claim form. In addition, if the billing structure is limited to the primary attributable diagnosis during a visit, these symptoms, which are often vague and prevalent in women > age 40, may not be reported on the claim form. These data also do not currently capture symptom-related details on frequency, duration, and whether this symptom was ongoing or an incident event, which previous research has suggested may be important.

There are several key unknown factors that may affect the cost-effectiveness results. There is little information on how quickly ovarian cancer spreads or the clinical benefit of being diagnosed a few months earlier. Further, nonmonetary costs associated with an FP, such as emotional distress, morbidity, and time taken off from work, were not included here.

Conclusions

This research and previous studies suggest that although many women may be experiencing the four highlighted symptoms, these symptoms are most prevalent in claims data in the 3 months before diagnosis. Abdominal or pelvic pain and bloating were more common than the other two symptoms before diagnosis. The usefulness of a claims-based screening program is limited by this short period of time, on average, between symptom and the time of diagnosis.

Although the ovarian cancer screening method presented here had limited performance, the approach could be used...
with different types of data. Electronic medical records are one key data source where a screening tool may be useful. The amount of information available for a screening tool will dramatically increase, potentially with symptom-specific details, which should better capture the overall patient experience. The passive screening method potentially could be used to identify other incident diseases cases if found to be effective with electronic medical records.

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Disclosure Statement

The authors have no conflicts of interest to report.

References

4. Vine MF, Ness RB, Calingaert B, Schildkraut JM, Berchuck A. Types and duration of symptoms prior to diagnosis of invasive or borderline ovarian tumor. Gynecol Oncol 2001;83:466–471.
11. Sensitivity and specificity of multimodal and ultrasound screening for ovarian cancer, and stage distribution of detected cancers: Results of the prevalence screen of the U.K. Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). Lancet Oncol Published online March 11, 2009.

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(Appendix follows →)
Appendix: Symptoms Defined by International Classification of Disease (ICD-9) codes

1. Pelvic or abdominal pain
   625.0 Dyspareunia
   625.5 Pelvic congestion syndrome
       Congestion-fibrosis syndrome; Taylor’s syndrome
   625.9 Unspecified symptom associated with female genital organs
   789.0* Abdominal pain
       Abdominal tenderness; colic: NOS, infantile; cramps, abdominal; epigastric pain; umbilical pain

2. Difficulty eating or feeling full quickly
   536.0 Achlorhydria
   536.9 Unspecified functional disorder of stomach
       Functional gastrointestinal: disorder; disturbance; irritation
   564.0 Constipation
   783.0 Anorexia; loss of appetite
   787.02 Nausea alone
   787.3 Flatulence, eructation, and gas pain
       Abdominal distention (gaseous); bloating; tympanites (abdominal) (intestinal)

   NOS, not otherwise specified.

   787.9 Other symptoms involving digestive system
       Tenesmus (rectal)
   787.91 Diarrhea
       Diarrhea NOS

3. Bloating
   789.3* Abdominal or pelvic swelling, mass, or lump
       Diffuse or generalized swelling or mass: abdominal NOS; umbilical

4. Urinary symptoms (urgency or frequency)
   788.1* Dysuria
       Painful urination; strangury
   788.3* Urinary incontinence
       Enuresis NOS; incontinence of urethral sphincter
   788.4* Frequency of urination and polyuria
       Frequency of micturition; nocturia