Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology Prioritising Summary

Ovarian Cancer Symptom Index

October 2007

AHTA

Adelaide Health Technology Assessment

ISBN
Publications Approval Number:

Electronic copies can be obtained from http://www.horizonscanning.gov.au

Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

DISCLAIMER: This report is based on information available at the time of research cannot be expected to cover any developments arising from subsequent improvements health technologies. This report is based on a limited literature search and is not a definitive statement on the safety, effectiveness or cost-effectiveness of the health technology covered.

The Commonwealth does not guarantee the accuracy, currency or completeness of the information in this report. This report is not intended to be used as medical advice and intended to be used to diagnose, treat, cure or prevent any disease, nor should it be used therapeutic purposes or as a substitute for a health professional's advice. The Commonwealth does not accept any liability for any injury, loss or damage incurred by use of or reliance the information.

The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from departments in all states and territories, the Australia and New Zealand governments; and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This Horizon scanning prioritising summary was prepared by Adrian Purins, Linda Mundy and Professor Janet Hiller from the National Horizon Scanning Unit, Adelaide Health Technology Assessment, Discipline of Public Health, Mail Drop 511, University of Adelaide, Adelaide, SA, 5005.

PRIORITISING SUMMARY

REGISTER ID: **000344**

NAME OF TECHNOLOGY: **OVARIAN CANCER SYMPTOM INDEX**

PURPOSE AND TARGET GROUP: **SCREENING OF WOMEN FOR OVARIAN CANCER**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☐	No	
☒	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
USA	✓		

IMPACT SUMMARY:

General practitioners or other medical personnel would administer the screening survey to female patients presenting with gastrointestinal or abdominal symptoms, which may indicate ovarian cancer.

BACKGROUND

Currently there is no effective method of screening for ovarian cancer and as such the first presentation of many women occurs at an advanced stage of the disease when the prognosis is poor. If ovarian cancer is diagnosed at Stage I when it is limited to the ovaries the prognosis for the patient is extremely good, with greater than 90 per cent survival (AHRQ 2006). Until recently it was accepted dogma that ovarian cancer caused no symptoms until the disease reached an advanced stage, however, there is a growing realisation that ovarian cancer causes a distinct pattern of, and timing of symptoms (Goff et al 2004). This summary investigates the evidence behind a recently reported ovarian cancer symptom index.

CLINICAL NEED AND BURDEN OF DISEASE

In 2002 ovarian cancer was the eighth most common cancer diagnosed in Australian women and ranked sixth in terms of cancer deaths in women. Over the past 25 years the annual age-standardised incidence of ovarian cancer has remained stable at 12-13 cases per 100,000 women. In 2002 there were 1,273 new cases of ovarian cancer and it was predicted that there would be 1,465 new cases in 2006 increasing to 1,645 in 2011. In 2004 the mortality rate for ovarian cancer was 7.5 deaths per 100,000 females with ovarian cancer being the underlying cause of death in 851 cases. The 5-year survival rate for ovarian cancer in Australia was 42.1 per cent in 2002 (AIHW 2006).

DIFFUSION

No evidence was found to indicate the diffusion of this program into the Australian health care system.

COMPARATORS

Currently, there are no high-quality, standard screening techniques for the routine early detection of ovarian cancer. Current methods in use in Australia include bimanual pelvic examination, transvaginal ultrasound, and serum CA-125[1] levels. There is only low quality evidence to support the use of these tests for the diagnosis of ovarian cancer and, currently, they do not meet the requirements for high quality screening tests (Anderiesz & Quinn 2003). Additionally, there are several areas of rapidly developing research into a variety of techniques for screening women for ovarian cancer. A report in 2006 identified four main approaches to a potential genetic screening tests for ovarian cancer diagnosis (AHRQ 2006);

- Tests involving a single gene e.g. the radioimmunoassay for CA-125;
- Tests for mutations in genes that may increase the risk of ovarian cancer;
- Tests looking for the expression of one or more genes that allow the differentiation of ovarian cancer patients from normal subjects; or
- Tests for protein expression levels that allow normal subjects and ovarian cancer patients to be distinguished, e.g. in the serum.

The report concludes that there is a lack of evidence for the effectiveness of these nascent techniques, no indication of patient benefits as yet and that it will be several years before these tests are established as mainstream screening tests (AHRQ 2006).

SAFETY AND EFFECTIVENESS ISSUES

At present there is a lack of specific pathology-based tests that can be used for screening women for ovarian cancer. Due to this fact there have recently been calls for the development of a clinically based index to assess women for any patterns of

[1] CA-125 is Cancer Antigen 125, a protein which is higher in the blood of some cancer patients and in particular is used for ovarian cancer detection, although the accuracy of this test for ovarian cancer screening is still being debated.

symptoms which may allow normal subjects to be differentiated from ovarian cancer affected women.

Evidence that early ovarian cancer caused symptoms was initially published in 2000 and consisted of the results of a survey of women who had ovarian cancer at a variety of disease stages. The study indicated that 95 per cent of ovarian cancer patients had symptoms preceding their diagnosis of ovarian cancer. The women who ignored the symptoms were more likely to have an advanced stage of disease at their diagnosis than the women who did not ignore their symptoms and sought clinical help (Goff et al 2000)[2].

In an effort to investigate the difference between normal women and ovarian cancer patients, with regard to symptoms, a case-control study questioned both women recently diagnosed with ovarian cancer (n=168) and normal control subjects (n=251) (Olson et al 2001). The women were interviewed about whether or not they experienced any of eight symptoms. Of the women with ovarian cancer, 93 per cent reported at least one symptom compared to 42 per cent of control women (Table 1). Women with ovarian cancer were more likely to have symptoms such as bloating and abdominal pressure (odds ratio = 25.3), a lack of appetite (odds ratio = 8.8) and abdominal or lower back pain (odds ratio = 6.2).

Table 1 Comparison of reported symptoms between ovarian cancer patients and normal controls

	Ovarian cancer cases (n=168)	Control subjects (n=251)	
	n (%)	n (%)	OR (95%CI)
Any Symptom	156 (93)	106 (42)	17.8 (9.4, 33.7)
unusual bloating, fullness, and pressure in the abdomen or pelvis	119 (71)	22 (9)	25.3 (15.6, 40.9)
Unusual abdominal or lower back pain	87 (52)	37 (15)	6.2 (4.0, 9.6)
Unusual lack of energy	72 (43)	40 (16)	3.9 (2.5, 6.1)
Frequent urination, urgency or burning	55 (33)	31 (12)	3.5 (2.2, 5.7)
Unusual constipation	36 (21)	18 (7)	3.5 (2.0, 6.3)
Unusual lack of appetite	34 (20)	7 (3)	8.8 (4.3, 18.2)
Unusual diarrhoea	27 (16)	15 (6)	3.0 (1.6, 5.7)
Nausea	21 (13)	22 (9)	1.5 (0.8, 2.8)
Other symptoms	59 (35)	19 (8)	6.6 (3.9, 11.2)

Adapted from (Olson et al 2001), OR = odds ratio

This study indicated that there were differences between women with and without ovarian cancer with regard to the symptoms reported to have occurred prior to diagnosis or interview.

Although the study by Olson et al (2001) reported a significant difference between women with and without ovarian cancer, the design of the study does not control for

[2] This study is a cross-sectional prognostic retrospective uncontrolled survey and was hence not of sufficient quality to be graded by the standard dimensions of evidence.

recall or selection bias which may have affected the outcomes. A more recent study, with a better design and more subjects, *prospectively* addressed the question of whether there is a difference between normal and ovarian cancer affected subjects (Goff et al 2004) (level IV aetiology evidence). A survey of symptoms was administered to 1,709 women attending primary care. The survey asked the subjects to rate the severity, frequency and duration of symptoms if they occurred. The major differences in reported symptoms between the women subsequently diagnosed with ovarian cancer and normal subjects are presented in Table 2.

Table 2 Symptoms occurring in women with ovarian cancer versus normal subjects

	Odds ratio Ovarian Cancer (n= 44) vs Normal Subjects (n= 1011)*
Increased abdominal size	7.4 ,95% CI [3.8-14.2]
Bloating	3.6, 95% CI [1.8-7.0]
Urinary urgency	2.5, 95% CI [1.3-4.8]
Pelvic pain	2.2, 95% CI [1.2-3.9]

* Some women were later diagnosed with irritable bowel syndrome. Adapted from (Goff et al 2004).

There was a greater odds of women with ovarian cancer having specific symptoms. In addition, there was a significantly higher severity and frequency of abdominal pain, pelvic pain, bloating, constipation, and increased abdominal size in women with ovarian cancer compared to normal subjects. The reference population in this study was typical of a potential screening population, women presenting to a primary care clinic with diverse and non-specific symptoms. This study showed that it was possible to distinguish women with ovarian cancer from non-cancer affected patients in this setting (Goff et al 2004).

A 2007 study surveyed a further 633 women, including 149 women with ovarian cancer, 255 healthy women at high risk[3] of ovarian cancer, and 233 women referred for pelvic/abdominal ultrasound (Goff et al 2007) (level III-2 diagnostic evidence). The aim of this research was to produce a symptom index which could be used as a screening tool for ovarian cancer. The control populations were chosen to minimise recall bias as they were likely to be as aware of, and therefore report with similar accuracy, pelvic/abdominal symptoms as the patients with ovarian cancer. The patients were divided into an exploratory group to define what factors could independently predict whether a patient had ovarian cancer and a confirmatory group on which the index was used to measure its sensitivity and specificity.

For the exploratory group several symptoms were found to be predictive of ovarian cancer. From these symptoms an index was constructed to be a screening tool for ovarian cancer. The model with the highest sensitivity was selected. The symptoms in this model consisted of pelvic/abdominal pain, increased abdominal size/bloating, and feeling full/difficulty eating. To be considered positive by this index the subject had to

[3] These women were already enrolled in an ovarian cancer screening group

report that any of these six symptoms had occurred for <12 months and >12 times per month. This index was then investigated in the confirmatory group (Table 3).

Table 3 Sensitivity and specificity of the ovarian cancer symptom index in a confirmatory population

	Sensitivity	Specificity
Women < 50 yrs	86.7%	86.7%
Women ≥ 50 yrs	66.7%	90%
Early stage patients	56.7%	n/a
Advanced stage patients	79.5%	n/a

Adapted from (Goff et al 2007)

The authors state that the symptom index should be used as an initial method to direct patients to further testing if they return a positive score on the index. The symptom index is currently being prospectively assessed in a primary care setting.

Although this evidence is preliminary, the symptom index developed by Goff et al has the potential to have a large impact on the detection of ovarian cancer as there is currently no adequate screening test for ovarian cancer, Despite this, the evidence needs to be supported by further large scale studies and the prognostic benefits, if any, must be investigated. There is some evidence that the symptom index may provide earlier detection of ovarian cancer, however whether this earlier detection will translate into patient benefit is not yet known. What is known is that patients who are detected at the early stages of ovarian cancer or patients that have no macroscopic disease after surgery have much higher chances of surviving ovarian cancer.

COST IMPACT

No cost impact information was found during the preparation of this summary.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

Currently there is no effective screening test for ovarian cancer, therefore the development of an effective question based symptom index would be an important clinical tool. The symptom index investigated here showed positive outcomes and further studies are underway to investigate the use of the index in a prospective manner.

HEALTHPACT ACTION:

The symptom index may be of use for the future development of Clinical Practice Guidelines for the diagnosis of women with ovarian cancer. Although HealthPACT

has recommended that further assessment of this technology is no longer warranted, the contents of this summary should be forwarded to the College of General Practitioners for their consideration.

NUMBER OF INCLUDED STUDIES

Total number of studies	
Level III-2 diagnostic evidence	1

REFERENCES:

AHRQ (2006). *Genomic Tests for Ovarian Cancer Detection and Management,* Agency for Healthcare Research and Quality.http://www.ahrq.gov/downloads/pub/evidence/pdf/genomicovc/genovc.pdf

AIHW (2006). *Ovarian cancer in Australia: an overview, 2006,* Australian Institute of Health and Welfare.http://www.aihw.gov.au/publications/can/oca06/oca06.pdf

Anderiesz, C. & Quinn, M. A. (2003). 'Screening for ovarian cancer', *Med J Aust,* 178 (12), 655-656.

Goff, B. A., Mandel, L. et al (2000). 'Ovarian carcinoma diagnosis', *Cancer,* 89 (10), 2068-2075.

Goff, B. A., Mandel, L. S. et al (2007). 'Development of an ovarian cancer symptom index: possibilities for earlier detection', *Cancer,* 109 (2), 221-227.

Goff, B. A., Mandel, L. S. et al (2004). 'Frequency of symptoms of ovarian cancer in women presenting to primary care clinics', *JAMA,* 291 (22), 2705-2712.

Olson, S. H., Mignone, L. et al (2001). 'Symptoms of ovarian cancer', *Obstet Gynecol,* 98 (2), 212-217.

SEARCH CRITERIA TO BE USED:

Early Diagnosis
Female
Humans
Ovarian Neoplasms/complications/ diagnosis
Questionnaires
Severity of Illness Index