Diagnosis of ovarian cancer in primary care
Persistent abdominal distension warrants urgent referral

Worldwide, more than 200 000 new cases of ovarian cancer occur each year, and these account for around 4% of all cancers diagnosed in women.1 Overall the five year survival rate from ovarian cancer is poor at around 30-40%. For women diagnosed with early stage disease, the five year survival rate is over 70%, but only a fifth of cases are diagnosed early.2 For women with late stage disease, the five year survival rate is around 15%. No effective screening test is available.

Earlier identification of symptoms could improve prognosis,3 4 and in the linked case-control study, Hamilton and colleagues report the predictive value of symptoms in diagnosing ovarian cancer in primary care.5

The late stage of presentation has been blamed on the insidious nature of the disease, which has vague non-specific symptoms. Historically, ovarian cancer has been referred to as the “silent killer” because it was believed that no symptoms were evident in early disease. Deciding which patients to refer to a specialist is difficult for primary care doctors because the presenting symptoms of ovarian cancer are similar to those of abdominal disease and gastrointestinal disease. This, coupled with the fact that primary care doctors on average see only one case of ovarian cancer every five years, means that more than half of women with ovarian cancer are not referred directly to gynaecological cancer clinics, thus delaying diagnosis.6 One study found that only 24% of women diagnosed with ovarian cancer were referred urgently.7

Over the past decade, several studies have disproved the “silent disease” myth, and research has intensified into using symptoms as a diagnostic tool.8 Furthermore, these studies have shown that symptoms are present in more than 90% of women with early stage disease, and that these symptoms may be present for up to 15 months before diagnosis (AWW Lim. Investigating the potential for expediting diagnosis of ovarian cancer via prompt symptom recognition and “targeted screening” [PhD thesis]. London: Queen Mary University, 2009). Women with ovarian cancer experience symptoms more frequently, severely, and persistently than women without the disease.3 6 These symptoms include persistent pelvic and abdominal pain, increased abdominal size or persistent abdominal distension (or both), and difficulty with eating or feeling full quickly.3 5 However, the methods used in most studies involve retrospective collection of data directly from women, a long duration between diagnosis and data collection, and the use of checklists. The data are therefore subject to recall, selection, and survivor bias.10

Although Hamilton and colleagues’ case-control study uses patients’ medical records and is therefore subject to recording bias, it is large enough to allow the calculation of positive predictive values (PPVs) in primary care for ovarian cancer for all important symptoms, individually and combined. All women aged 40 or more diagnosed with primary ovarian cancer during 2000-7 in 39 general practices in one area of England were included. The participants’ entire primary care records for one year before diagnoses were examined. The study is unique in that it calculated the risk of ovarian cancer across the range of key symptoms and was based in primary care where diagnostic delays are prevalent.

PPVs are measures of the likelihood of a woman with certain symptoms having ovarian cancer. Using multivariable analysis, seven symptoms were associated with ovarian cancer. These were abdominal distension (PPV 2.5%, 95% confidence interval 1.2% to 5.9%), postmenopausal bleeding (0.15%, 0.2% to 0.9%), loss of appetite (0.6%, 0.3% to 1.0%), increased urinary frequency (0.2%, 0.1% to 0.3%), abdominal pain (0.3%, 0.2% to 0.3%), rectal bleeding (0.2%, 0.1% to 0.4%), and abdominal bloating (0.3%, 0.2% to 0.6%). Around 85% of cases and 15% of controls had reported at least one of the seven symptoms to primary care before diagnosis. After excluding symptoms reported in the 180 days before diagnosis, abdominal distension, urinary frequency, and abdominal pain remained independently associated with a diagnosis of ovarian cancer.

Only persistent abdominal distension had a PPV over 1%. The low PPVs reflect the high frequency of abdominal symptoms in the population, together with the relatively low incidence of ovarian cancer. The finding of a PPV of 2.5% for persistent abdominal distension means that it carries the highest risk. It was reported by a third of women with ovarian cancer and, importantly, was equally as common in stages I and II cancer as in advanced disease.

The related term, “bloating,” is used by women for both persistent and intermittent abdominal distension. Studies have found that bloating is associated with ovarian cancer, and that it was the most common symptom in women with early stage disease.11 However, the studies did not distinguish between persistent abdominal distension and intermittent bloating. A subsequent study found that 38 of 44 women with ovarian cancer had persistent abdominal distension in contrast to bloating, which was present in only two of these women.12 Persistent abdominal distension is not included in the current UK guidance for urgent referral.12 It is clearly a
common and important symptom and warrants urgent referral.

The diagnosis of ovarian cancer will continue to be a challenge for primary care doctors. More research, particularly prospective studies, is needed to improve our knowledge of the predictive value of different symptoms in ovarian cancer. In this respect, the prospective validation of the Goff index, and a prospective study evaluating symptoms in apparently healthy women participating in the UK ovarian cancer screening trial, are eagerly awaited. What is important for both women and primary care doctors is that ovarian cancer can no longer be regarded as a silent killer.


Should healthcare workers have the swine flu vaccine?

Evidence from decades of seasonal vaccination suggests likely benefits and low risk of adverse events

The first batch of vaccine for the influenza A/H1N1 2009 “swine flu” pandemic should be ready and licensed by October, and the United Kingdom’s government has ordered enough vaccine for each person to receive two doses. Because vaccine production will take several months to complete, a prioritisation plan has just been announced, and frontline healthcare workers will be among the first to be offered vaccination. The potential benefits of influenza vaccination for healthcare workers are threefold—personal protection, protection of patients, and reduction of absenteeism. There is good evidence that among healthcare workers a well matched seasonal vaccine is 85-90% effective in preventing serologically confirmed influenza, that it indirectly protects elderly patients in some settings, that it may reduce absenteeism, and that it has limited and mild adverse effects.

Despite this, uptake of seasonal flu vaccine among healthcare workers has consistently been low (in winter 2008-9 only 16.5% of healthcare workers in England received the vaccine). So will uptake be any different during a pandemic?

More than 75% of healthcare workers responding to a survey in Leicester, UK, indicated willingness to accept a pandemic vaccine. However, this survey was conducted when the main pandemic risk appeared to be H5N1, which is associated with a high case fatality rate, rather than the current H1N1 strain, which is associated with relatively low mortality. In the linked study, Chor and colleagues show that, in a sample of 2255 healthcare workers in Hong Kong hospitals, the intention to accept pre-pandemic vaccines increased from 28.4% for H5N1 vaccine during the World Health Organization alert phase 3 to 47.9% for H1N1 at phase 5. An online poll just conducted by the Nursing Times reports that 37% of frontline nurses who replied were currently planning to be vaccinated, 33% were undecided, but 30% were not planning to be vaccinated. In line with surveys of seasonal flu vaccine uptake, intended acceptance of pre-pandemic or pandemic flu vaccines was associated with receipt of previous seasonal flu vaccines, perceived likelihood of being infected, and belief in the efficacy of flu vaccines. Reasons for refusing the vaccine included concerns about safety and efficacy, and low perceived threat of a pandemic.

Can we be sure that the new pandemic H1N1 vaccine will be as effective and safe as seasonal flu vaccines? The European Commission has already approved four “mock-up” vaccines developed by Baxter, GlaxoSmithKline, and Novartis on the basis of earlier immunogenicity and safety data generated with H5N1 virus strains. These mock-ups were developed knowing that the virus strain would be different in the event of a pandemic, and altogether they have been tested in more than 8000 people. The European Medicines Agency states that “decades of experience with seasonal influenza vaccines indicate that insertion of a new strain in a vaccine, as will apply with the change from H5N1 to H1N1 in the mock-up vaccines, should not substantially affect the safety or level of protection offered.” Two doses of an adjuvanted H5N1 vaccine have been shown to reach the licensing criteria for immunogenicity while maintaining an antigen sparing approach and to be cross protective across different clades of H5N1. Trials to evaluate immunogenicity and safety with the new H1N1 antigen inserted in the mock-up vaccines are currently under way, and these results will inform licensing decisions.
A particular concern for recipients may be the association of the 1976-7 swine flu vaccine with Guillain-Barré syndrome, with an attributable risk of around 12 cases per million vaccinations. This rare event has decreased greatly during the past 15 years (to around 0.7 reports/million vaccinations). Indeed, recent research suggests no significant increase in the risk of this syndrome after vaccination, but a greater risk after natural influenza infection. Thus, even if the vaccine was associated with a small increase in the risk of the syndrome, this would probably be outweighed by a protective effect against flu related Guillain-Barré syndrome. However, as with all new drugs, post-marketing surveillance (including for Guillain-Barré syndrome) is the only way to identify rare adverse events.

Healthcare workers in England are being urged to be vaccinated against pandemic and seasonal flu as soon as possible to protect themselves and their patients. NHS chief executives are also being directed to ensure maximum uptake. Implementation of the pandemic flu vaccination programme should take on board the lessons learnt from research on vaccination for seasonal flu—simple education and promotion and onsite clinics have not achieved high vaccination rates, but the additional use of convenient mobile systems, monitoring and feedback systems, and “opt-out” systems (where healthcare workers need to indicate their reasons for not accepting the vaccine) show promise.

In a pandemic there are many uncertainties, but without vaccination many healthcare workers will become infected. Although this will be a mild illness for most, deaths in previously healthy young adults have occurred. Flu vaccination is likely to reduce this risk and has a well understood safety profile. Vaccination may also help to keep the healthcare system operating at maximum capacity throughout the pandemic.

The use and abuse of alcohol in society is complex. Although international evidence shows that the main drivers of consumption are price and availability, there are many other factors that are deeply embedded in society and individual behaviours that influence how, why, and how much people drink. A recent report from the BMA, *Under the influence—the damaging effect of alcohol marketing on young people*, provides a fascinating overview of the links between advertising, promotion, and consumption. Its main author, Gerard Hastings, is the first professor of social marketing in the UK and is clearly disturbed by the accumulating evidence on the links between the £800m (£915m, $1.13bn) spent annually by the alcohol industry on marketing and the nation’s consumption. The report’s analysis of the evidence confirms that alcohol marketing is independently linked to the age of onset of drinking in young people and the amount they drink. These factors are also predictors of alcohol problems in later life. Reports from Anderson and colleagues and the European Commission had similar conclusions. How are young people exposed to alcohol promotion? *Alcohol Concern* showed a peak of television advertising of beer and spirits in the late afternoon and early evening, whereas wine advertising peaked later. In cinemas alcohol advertising takes place where films are classified for children under 12. Even within non-advertising broadcasts, alcohol frequently plays a part in ordinary events.

### Alcohol and social marketing

**Is it time to ban all forms of marketing?**

The use and abuse of alcohol in society is complex. Although international evidence shows that the main drivers of consumption are price and availability, there are many other factors that are deeply embedded in society and individual behaviours that influence how, why, and how much people drink. A recent report from the BMA, *Under the influence—the damaging effect of alcohol marketing on young people*, provides a fascinating overview of the links between advertising, promotion, and consumption. Its main author, Gerard Hastings, is the first professor of social marketing in the UK and is clearly disturbed by the accumulating evidence on the links between the £800m (£915m, $1.13bn) spent annually by the alcohol industry on marketing and the nation’s consumption. The report’s analysis of the evidence confirms that alcohol marketing is independently linked to the age of onset of drinking in young people and the amount they drink. These factors are also predictors of alcohol problems in later life. Reports from Anderson and colleagues and the European Commission had similar conclusions.

How are young people exposed to alcohol promotion? *Alcohol Concern* showed a peak of television advertising of beer and spirits in the late afternoon and early evening, whereas wine advertising peaked later. In cinemas alcohol advertising takes place where films are classified for children under 12. Even within non-advertising broadcasts, alcohol frequently plays a part and is usually portrayed in a positive light, all coming together with careful product design, pricing, placement, and distribution, to distort the social norms. It is the newer and more insidious forms of marketing that have not yet been properly assessed but are likely to be most influential on adolescents—the internet, mobile phone messages, sports and festival sponsorship, merchandising and social networking sites—the list is growing. The report highlights the huge awareness of drink brands by young people. Over 90% of 13 year olds could identify the brand of popular products.
Improving adherence to prescribed drugs

Techniques used to change behaviour should be considered

Abilio de C Almeida Neto
associate professor, Faculty of Pharmacy, University of Sydney,
NSW 2006, Australia
Parisa Aslani
senior lecturer, Faculty of Pharmacy, University of Sydney,
NSW 2006, Australia
Timothy F Chen
senior lecturer, Faculty of Pharmacy, University of Sydney,
NSW 2006, Australia
Competing interests: None declared.
Provenance and peer review: Not commissioned; externally peer reviewed.

Cite this as: BMJ 2009;339:b3282
doi: 10.1136/bmj.b3282

Non-adherence to prescribed medicines can cause treatment failure, mortality, and increase healthcare costs.1 2 Methods of improving adherence are only marginally effective,3 so several challenges remain.

Recently the National Institute for Health and Clinical Excellence (NICE) published a clinical guideline for involving patients in decisions about prescribed drugs and increasing adherence.4 The guideline recommends that prescribers accept the patient’s right to decide not to take a drug, even when they do not agree with the decision, “as long as the patient has capacity to make an informed decision and has been provided with the information needed to make such decision.” However, it fails to provide guidance for dealing with circumstances in which refusal to accept medication places the patient at an unacceptable risk of harm. Despite this shortfall, the guideline outlines useful strategies that may improve adherence to drug treatment.

The guideline promotes active yet sensitive provision of information and discussion. It encourages prescribers to explore and understand patients’ perspectives and the reasons why they may not want to, or are unable to, take the prescribed drug. The main recommendation is to involve patients in decisions about drugs they are prescribed, while recognising that this could result in patients deciding not to take them. Interventions should be tailored to the needs of the individual patient.

Although the rights of patients to make decisions about their own health is indispensable in modern clinical practice, recommendations should also consider

Doctors need better support in dealing with work related medical problems

Dame Carol Black’s report Working for a Healthier Tomorrow strongly advocates changes in the arrangements for sickness certification to promote better health of the working age population in the United Kingdom. The report states that current social security systems encourage people to stay off work until they are fully medically fit to return to their job. This policy increases the risk of long term disability and subsequent loss of employment.

General practitioners are usually the first healthcare professionals that employees encounter when they are off sick from work. After seven days of absence from work because of illness, employers can request a sick note from the employee, so they can claim statutory sick pay. Employees will usually seek advice from their general practitioner regarding their fitness to return to work. Herein lies the problem. General practitioners feel that they are the patients’ advocates and thus have to follow their patients’ wishes. Few general practitioners think that signing a sick note might have a deleterious effect on their patients’ health.

In her report, Dame Carol recommended that the current paper based sick note should be replaced by an electronic “fit note.” The aim is twofold. Firstly, to shift the focus of the advice from what people can’t do to what they can do, thereby facilitating their retention in the workplace. Secondly, to enable improvements in data collection and hence trend analysis, which in turn will facilitate public health planning.

The government responded to the report positively, and a draft fit note has been piloted by the Department for Work and Pensions. The draft form has an option...
for doctors to state whether the person is fit for some work, and if the person would benefit from a phased return to work, altered hours, amended duties, or adaptations to the workplace.

Evidence is available to support such a change in the sick note. We know that the advice of healthcare providers is an important component of rehabilitation after illness. Furthermore, evidence exists that adaptations to the workplace improve the rate of return to work and prevent long term disability for serious and less serious illnesses, but the effects on health outcomes are unclear.

Experience in Scandinavian countries has shown that it is not easy to increase the uptake of partial return to work, probably because of inflexible work arrangements and poor collaboration between stakeholders. This means that, despite the pilot form being well received by stakeholders and general practitioners, there are still many obstacles to ensuring that the new fit note improves the health of the working age population. Employers and employees must be prepared and willing to sit together and discuss the adjustments to working hours or duties recommended by the general practitioner. For more difficult cases, employers may need support from occupational health professionals.

It is often argued that a clear business case for occupational health interventions is essential to improve the uptake of occupational health measures by employers. The draft consultation on the fit note regulations includes a cost-benefit analysis of the proposed certificate for general practitioners but not for employers.

In drafting their consultation paper, the Department of Work and Pensions has assumed that most employers would prefer an employee to be at work even in a limited or supernumerary capacity than to pay for them to be at home on sick pay. But, curiously, the financial benefit for firms has not been measured because, as the report states, it is too difficult to assess.

Given the uncertainty as to whether employers will have sufficient financial incentives to accommodate the partial return to work of their employees, the government should consider other incentives, such as legislation. For example, in the Netherlands, the employer and employee have a legal obligation to sit together and discuss solutions to obstacles preventing return to work. This is seen as an important element in the decrease of long term disability in the country.

General practitioners and other healthcare professionals not trained in occupational health still feel uncomfortable about assessing fitness for work, especially as they usually have no access to their patient’s employer. Many general practitioners would like access to specialist occupational health advice via the NHS. We advocate that the new certificate includes the option to recommend referral for an occupational health assessment. Doctors need better support in decision making on work related medical problems. Therefore, we strongly recommend that work related aspects, such as return to work, are included in all clinical guidelines.

The new fit note requires a change in legislation, and the draft regulations are currently at the consultation stage, with a view to them coming into force in early 2010. But a fundamental change in the perceptions and beliefs of employers, employees, and healthcare professionals will be of paramount importance to the fit note achieving its aim.