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Screening for gynaecological conditions

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Summary
Well-organised cervical screening programmes have reduced the mortality from cervical cancer by up to 50% in the developed world. Despite the successful development of human papilloma virus vaccines, there is likely to remain a need for cervical screening for the foreseeable future. In contrast, the value of mass screening for ovarian cancer remains unproven, although current screening methods can detect early-stage disease in asymptomatic individuals. Breast screening does appear to be associated with a reduction in mortality in the long term but paradoxically may increase death rates in young women in the short term. Testing for sexually transmitted infections is effective in reducing morbidity but tends to be selective at present because of concerns over the cost and psychosocial implications of general population screening.

Introduction

Screening is defined as a procedure to help to identify, in an organised way, a specified disease or condition among asymptomatic individuals. Screening programmes may be applied to a general population or targeted at specific groups that are considered to be at particular risk. The aim is to detect disease early in order to facilitate effective treatment. Effective screening offers improved prognoses for some cases, less radical treatment for others and potential resource savings for society.

Screening, however, also has its limitations. It is important that people have realistic expectations of what a screening programme can deliver. Screening can reduce the risk of developing a condition or a condition's complications, but it cannot offer a guarantee of protection. In any screening programme, there are an irreducible minimum percentage of false-positive results (patients who are wrongly reported as having the condition) and false-negative results (when patients are wrongly reported as not having the condition). Screening may lead to longer morbidity for cases in which the prognosis is unaltered or to the overtreatment of questionable abnormalities. It may lead to false reassurance in the case of false-negative results, or anxiety and hazard for false-positive cases. Low-technology tests have low specificity, burdening already hard-pressed secondary care facilities with patients who have non-life-threatening conditions.

Box 1 lists some of the criteria desirable for an effective screening programme. There should, before the proposed screening programme is introduced, ideally also be evidence from a good-quality randomised controlled trial, analysed on an intention-to-treat basis, that the programme is effective in reducing mortality. To assess whether a screening test is reliable and valid, independent standards of reference are measured. Sensitivity is defined as the proportion of

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Box 1 Criteria for the desirable characteristics of a successful screening programme

1. The condition being screened for should represent a significant cause of mortality and have a significant prevalence in the population.
2. An accepted treatment must be available for the latent or early phase of the condition that improves outcome.
3. The facilities for diagnosis and treatment must be available.
4. A latent or early symptomatic stage must exist.
5. A sensitive and specific screening test must be available.
6. The test must be acceptable to the population.
7. The natural history of the condition should be well characterized.
8. An agreed treatment policy must exist.
9. Screening should be cost-effective.
10. Case-finding must be a continuous process.

individuals with the target condition who screen positive. A high sensitivity implies that a large proportion of individuals with the target condition have a positive result on the screening test. Specificity is defined as the proportion of individuals without the disease who have a negative result on the screening test. A high specificity reflects a low proportion of people falsely labelled as having the disease when they are in fact disease-free. Predictive values are important in clinical practice as they are the probabilities that someone testing positive really has the condition and someone testing negative does not. The positive predictive value is the proportion of people with a positive test who have the target disorder; the negative predictive value is the proportion of people with a negative test who do not have the target disorder.

Gynaecological cancers

Gynaecological cancers account for a sixth of female cancers, with an estimated 942,000 new cases worldwide per year. With increased life expectancy, the early diagnosis and prevention of cancer is an increasingly important issue. The possibility of reducing mortality by detecting cancer in the pre-invasive or early invasive stages is being pursued by constantly advancing technologies. Important aspects of screening, including psychological impact, cost–benefit ratio and uptake are receiving better attention. Genetic testing is now in place in clinical gynaecology to identify women at an increased risk of gynaecological cancer.

Ovarian cancer

Four thousand deaths occur every year in the UK from ovarian cancer, making it the fourth most common cause of female cancer death. The annual incidence of ovarian cancer in the general population increases with age to 40 per 100,000 in women aged over 45 years. The lifetime risk of developing the disease has increased from 1 in 70 to 1 in 55 over the past 30 years. Although the 5-year survival for patients diagnosed with stage I disease is more than 80%, this falls to 22% and 14% for stages III and IV disease, respectively. Despite the good prognosis for early-stage disease, the overall 5-year survival rate is less than 35%, largely because most patients have disease that has spread outside the ovary by the time of clinical presentation.

The aim of screening is the detection of asymptomatic early-stage disease. Unlike cervical cancer, no precursor lesion has been identified, and direct inspection of the ovaries is not possible without surgical intervention. Furthermore, the natural history of the condition is not well characterised. The relatively low prevalence of the disease means that any screening test must have high specificity to avoid unnecessary surgical interventions. For example, in order to have a positive predictive value of 10% or better for the general population aged over 50, a screening test for ovarian cancer would need to have specificity of at least 99.6%. Screening for ovarian cancer by bimanual palpation has a poor sensitivity and specificity, and is not recommended. Current screening strategies are based on serum tumour markers or ultrasound imaging of the ovaries.

Tumour markers

Serum CA-125 remains the most used tumour marker in ovarian cancer screening. CA-125 is a large glycoprotein of unknown function that is expressed during normal foetal development and by more than 80% of epithelial ovarian cancers. Serum levels are not affected by abdominal or pelvic examination but are increased in a number of benign conditions, such as endometriosis, uterine leiomyoma and pelvic inflammatory disease, as well as with malignancies of the breast, liver, lung and pancreas.

In asymptomatic women, measurement of serum CA-125 is unsuitable as a single screening test for ovarian cancer in premenopausal women due to its low sensitivity (50%) for stage I of the disease and poor specificity (98.5%). In the post-menopausal age group, although approximately 2 out of 3 cases of ovarian carcinoma could be detected by annual serum CA-125 measurement, only one-third would be detected in the early stage. About 80% of the pelvic masses will be classified correctly if cut-off values of 65 and 35 U/ml are used in premenopausal and post-menopausal women, respectively, with a pelvic mass.

The risk of developing ovarian cancer in a post-menopausal woman with an elevated serum level of CA-125 but a normal ovarian ultrasound scan is similar to that of the