

I wake up screening - an editorial meander

What screening should be part of a mature well-woman consultation?

Screening by asking

Does a series of direct questions constitute screening?

Most certainly it does, but clinical acumen is required to delve with sensitivity into your patient's habits, concerns, safety issues and other aspects of patient/doctor enquiry which makes for a professional relationship and is established over time. Such knowledge underpins all interactions and is the glue that bonds every consultation.

But verbal screening in women older than 50 years for general health matters, is more nuanced.

Wider issues to consider are:-

- partnership well-being - any domestic or inter-personal matters you wish to raise?
- age-related changes - menopausal symptoms, urinary issues, sexuality questions?
- mental health - any concerns about memory/forgetfulness, executive function e.g. driving ([Redelmeier et al JAMA Netw Open 2024;7:e248856](#)) or managing finances? ([Karlawish JAMA Netw Open 2022;5:e2231442](#)).
- Is your weight stable, is your diet healthy?
- does the patient have the financial means to cover expenses? ([Pisu et al Nat Rev Dis Primers 2022 doi 10.1038/s41572-022-00341-1](#)).

Vaccinations

Is it a Menopause Specialist's obligation to address vaccinations?

Yes, and even more pertinently now that new data are appearing about vaccine developments.

Shingles vaccination

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The varicella-zoster virus which causes chicken pox is also the cause of shingles. The virus can exist silently in nerve fibres and can be activated many years after the initial viral infection. This manifestation occurs as a rash followed by blistering along the roots served by the infected virus. Herpes-zoster and the resultant pain can be incapacitating (post-herpetic neuralgia) but prevention is available through a recombinant zoster vaccine.

The vaccine's effectiveness diminishes following a single shot from 70% in year one to around 50% in subsequent years. The effectiveness can be markedly improved by a booster dose given at least 2 months after the initial injection, to around 75% which lasts for at least 4 years ([Zerbo et al Ann Int Med 2024 doi 10.7326/M23-2023](#)).

The vaccine is highly recommended for anyone over the age of 50 years since the incidence of attacks increases with age. The relief from recurrent episodes is huge and the "value for money" highly positive ([Vargas Medscape 2024](#)).

Respiratory Syncytial Virus vaccination

The seriousness of Respiratory Syncytial Virus (RSV) infections can be judged by the conclusion of a study from the US which found that in "hospitalized adults with RSV infection, 22% of patients experienced an acute cardiac event, most often acute heart failure" ([Woodruff et al JAMA Intern Med 2024 doi 10.1001/jamainternmed.2024.0212](#)).

More encouraging results came from an investigation into an RSV vaccine trial that stated: "A single dose of the mRNA-1345 vaccine resulted in no evident safety concerns and led to a lower incidence of RSV-associated lower respiratory tract disease and of RSV-associated acute respiratory disease than placebo among adults 60 years of age or older." ([Wilson et al NEJM 2023;389:2233-44](#)).

Human Papilloma Virus vaccination

Your editor, in his youth, worked in a cytology laboratory and in a hospital that dealt with large numbers of patients suffering from cervical cancer. It remains a dream to witness the eradication of this affliction but it will take considerable political motivation to make inroads into the geographical and financial barriers that exist in vaccinating the most vulnerable.

The economic case for the upliftment of women's health is compelling, and a world-wide HPV vaccination drive would be a pragmatic and welcome flagship project. A *BMJ* article says "Closing the gender health gap by 2040 could add almost £39bn to



the UK economy and give each British woman around 9.5 more days of good health a year. That's according to data shared with *The BMJ* by the McKinsey Health Institute, whose recent report with the World Economic Forum describes investing in women's health as a \$1tn global opportunity, with a \$3 return on investment for every \$1 spent." ([Graham BMJ 2024;385:q787](#)).

There are calls for initiatives, for example "Science and Sex—A Bold Agenda for Women's Health" [Johnson JAMA Intern Med 2024;184:461-2](#)). Could we, as the promoters of women's health, not start in a most modest way and ask every woman we consult with, the following question:-

"Have you, your children and grandchildren had their HPV vaccinations?"

This way we - and our patients - could raise awareness and move the needle in the right direction.

Screening for cancer

What cancers should we screen for in postmenopausal women?

This topic is for national or international organisations to determine.

Your editor has often wondered who actually is responsible for recommending standard practice. We in O&G have International (WHO and FIGO) plus national organisations of major influence (ACOG, RANZCOG, RCOG and SAMS), and local societies which are agile to the needs and realities of the women we serve.

Sometimes it devolves to the courts to decide, for example, does the omission of a screening test amount to negligence on the part of the person's health-carer? In real life it is more complex than that with many forces in play that affect involvement in a cancer screening programme. Screening programmes are not subject to any form of regulation and many businesses profit handsomely from what they offer, irrespective of evidence of its effectiveness - never mind cost effectiveness. This is particularly true of the new liquid biopsies.

Cervical cancer. Cervical cytology smears are the supreme example of how screening tests *should* be developed. George Papanicolaou, with Mrs P's long-suffering assistance - (*personal communication from Jorg Kemper, Australia*) proved the initial value of testing with later explanations of the viral precipitating factors and ultimately preventative pathways. Other cancer tests lack the veracity of such underpinning aetiologies, progression tracking or preventative pathways. Harald zur Hausen discovered the causative mechanism through his work on the human papillomavirus, which made it possible to provide the route to prevention.



There are pre-malignant phases of cervical intra-epithelial neoplasia and Grade 2 CIN is recognised as a spontaneously reversible condition. Observational studies reveal that regression to normal occurs in about half of all cases and in young women with reproductive prospects, there is an option to monitor these patients with “active surveillance”. This is critical for screening as most women acquire HPV infection following their sexual debut before 25 years old but normal defence mechanisms deal with and clear the infection, which is the rationale for not recommending screening (with HPV or cytological testing) prior to this age. The actual “age of recruitment” can be 21 (historically), or 25 or 30 depending on each country’s regulations. Recurrent HPV infections with aggressive types (16,18 etc), together with aggravating factors, such as smoking or other causes of reduced immune efficacy, produce the circumstances of progression to invasive disease.

With repeated negative HPV screening, the interval between tests can be extended for women whose circumstances remain unchanged. By the time a patient is postmenopausal, with a series of negative tests it may be deemed unnecessary for to have repeated screening. This will be for expert committees to decide and as vaccinated women reach screening age, policies will again need revision.

In the United States there are various authoritative bodies who pronounce on these matters, such as the ACOG, the American Cancer Society plus the [US Preventive Services Task Force](#), which is updating its recommendations at present.

Editorial comment. The cytology of exfoliative cells from the genital tract can include debris from the fallopian tubes, which may be where ovarian cancers originate. As such, some Pap smears have been shown to contain malignant serous cancer cells from the ovary years prior to the primary being found ([Paracchini et al](#) Sci Transl Med 2023 doi 10.1126/scitranslmed.adi2556). This, however, will not be a reliable form of ovarian malignancy screening, so suspicions need to be raised if recurrent general abdominal symptoms, lassitude and weight loss occur, as described by [Barber](#) (Br J Nurs 2024 doi 10.12968/bjon.2024.33.5.S16). Liquid biopsy technology is most likely to provide this break-through. Preliminary data on combining cell-free DNA fragment diagnostics with the biomarkers CA125 and HE4, seem the most promising ([Otto](#) Medscape 2024).

Screening developments

Screening mammography for breast cancer

Those who advocate mammography as a screening test for breast cancer will have noted the US Preventative Services Task Force’s change in their recommendations

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for women of average risk. The starting age is lowered to 40 years and biennial scanning retained till the age of 74 years, beyond which they say there is insufficient evidence to assess the benefits to harms ratio ([USPSTF JAMA 2024 doi 10.1001/jama.2024.5534](#)).

Enthusiasts of mammography (which excludes your editor) will find the arguments in favour of more intense screening explained by an American expert ([Berg JAMA Oncol 2024 doi 10.1001/jamaoncol.2024.0905](#)). The article commends the inclusion of regular mammographic screening from age 40, but argues for annual rather than biennial screening, especially for younger women and those from minority groups who face higher risks. It also emphasises the importance of addressing dense breast tissue, which can obscure cancer detection on mammograms, recommending supplemental MRI screening for high-risk individuals.

Recent studies are highlighted showing the effectiveness of MRI and other modalities like contrast-enhanced mammography, which the USPSTF guidelines fail to adequately consider. Overall, it advocates for a more comprehensive approach to breast cancer screening that addresses the needs of diverse populations and considers advanced screening technologies.

Screening for colorectal cancer - CRC

Should screening for colorectal cancers form part of a menopausal specialist's repertoire?

Colorectal cancer is the third commonest cause of death of all malignancies.

Screening should be offered to peri- and postmenopausal women because:

- CRC incidence rates rise from 45 years to the early seventies, when it is concluded "with high certainty" that it has substantial net benefit ([US Preventive Services Task Force JAMA 2021;325:1965-77](#))
- Screening can discover precancerous lesions which can be treated and avoid progression to invasive cancer
- Early stages can be found when management can be instituted which offers better survival rates than the treatment of late-stage disease

Considerable progress has been made in colorectal cancer screening and gynaecologists should be *au fait* with developments, so what follows is applicable as of the first quarter of 2024.

There are 3 modes of screening for CRC

1. Stool tests
2. Colonoscopy - direct visualisation



3. Blood tests – liquid biopsies

1. Stool tests.

These tests are the backbone of CRC screening programmes because of their availability, low cost and convenience. They require only testing kits and can be done in doctors' consulting rooms (or self-collected at home), with rapid results and acceptability.

Additionally they are becoming more technically sophisticated, but the established stool tests are:-

- Faecal occult blood tests
- Faecal immunochemical tests

Faecal occult blood tests detect blood in a stool sample using chemical methods.

Faecal immunochemical tests detect blood in a stool sample using antibody methods.

The former is done annually and the latter 3 yearly.

The rationale is that colon cancer – or its precancerous precursors – will shed blood into the faeces which the test will detect, triggering a colonoscopy.

However, discoveries that the genetic variations of DNA sequencing (comparing tumour cells and benign cells) can distinguish the malign from the normal in blood, has created the whole new field of liquid biopsies. This technology can now be applied to stool samples which contain sloughed colon tumours cells that can be identified, thus increasing screening accuracy. These are called multitarget stool RNA or DNA tests ([Barnell et al JAMA 2023;330:1760-8](#) & [Imperiale et al NEJM 2024;390:984-93](#)). Costs, which at present are considerable, and further information about the value of these tests in identifying precursor lesions, await clarification.

2. Colonoscopy

Direct visualisation tests to screen for colorectal cancer include colonoscopy, flexible sigmoidoscopy and CT colonography. Only the first offers therapeutic adenoma removal at the time of the procedure and is regarded as the gold standard of CRC screening.

The received wisdom is that colonoscopic screening for colorectal cancer should be initiated at age 50 years and be repeated at 10 yearly intervals thereafter. However



the “magic number” of 10 years has been challenged by work from Germany ([Heisser et al JAMA Intern Med 2023;183:183-90](#)).

and Sweden looking at outcomes following a negative test in a cohort of more than 100,000 citizens without a family history of CRC ([Liang et al JAMA Oncol 2024 doi 10.1001/jamaoncol.2024.0827](#)).

In an accompanying editorial the reasoning for this extended interval is enunciated, based on the natural history of the disease ([Lui et al JAMA Oncol 2024 doi 10.1001/jamaoncol.2024.0249](#)).

3. Blood tests - liquid biopsies

As expounded in sister publications to *Menopause Matters*, liquid biopsies are one of the most exciting contributions of genetic technology to medicine. However, their place in the field of screening has yet to be established and CRC falls into this category, despite recent research being published ([Chung et al NEJM 2024;390:973-83](#)).

Editorial opinion: There are a plethora of screening tests for the early detection of CRC and explaining the options to patients is demanding. The gold standard is colonoscopy but the procedure is intimidating and expensive. The new data about the interval between colonoscopies may swing the pendulum in its favour because of the extended “clean bill of health” now offered from 10 to 15 years. I believe the best screening is ultimately “the one that gets done” and for me that would be long-interval colonoscopy.

Your editor hopes that the office-bearers of Menopause organisations will continue to contribute to their members edification with updated screening recommendations.

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