

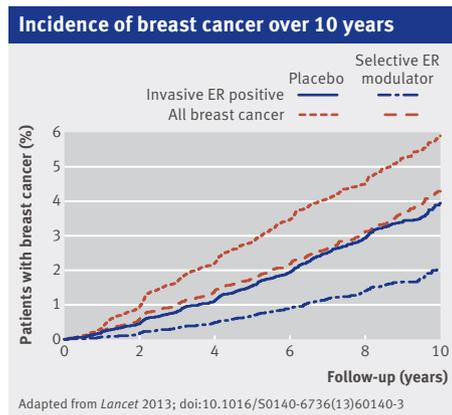
RESEARCH

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RESEARCH NEWS All you need to read in the other general medical journals Alison Tonks, associate editor, *BMJ* atonks@bmj.com



Pros and cons of drugs to prevent breast cancer

Pooled analyses of individual participant data from nine randomised trials have confirmed that selective oestrogen receptor (ER) modulators help prevent breast cancer in healthy women. Together, tamoxifen, raloxifene, arzoxifene, and lasofoxifene reduced the cumulative incidence of breast cancer by an estimated 38% relative to placebo in average or high risk women (4.2% v 6.3%; hazard ratio 0.62, 95% CI 0.56 to 0.69; number needed to treat 42). The protective effect was confined to cancers sensitive to oestrogen, and seemed to last for at least five years after the end of treatment. The drugs did not reduce mortality from breast cancer or other diseases, although they did reduce women's risk of fractures, particularly vertebral fractures (0.66, 0.59 to 0.73).

All agents caused a significant excess of venous thromboembolic events. Tamoxifen in particular was associated with extra endometrial cancers (hazard ratio 2.18, 1.39 to 3.42). So, although these drugs work, they are not harmless, and the balance of risks and benefits will depend on a woman's age, race, predicted risk of breast cancer, and whether or not she still has a uterus, says a linked comment (doi:10.1016/S0140-6736(13)60443-2). Predicting risk of breast cancer in well women is an inexact science, and women urgently need a convenient biomarker to help target preventive treatment at those with the most to gain and least to lose. Breast density is the most promising candidate so far, says the comment.

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Prophylactic penicillin cuts risk of recurrent cellulitis

Prophylactic penicillin almost halved the incidence of recurrent cellulitis in a recent placebo controlled trial (22% (30/136) v 37% (51/138); hazard ratio 0.55, 95% CI 0.35 to 0.86). A dose of 250 mg twice a day delayed the first episode after randomisation by 94 days overall but worked best during active treatment, which lasted one year. Protection waned once treatment stopped, and recurrence occurred during the next two years in just over a quarter of each group. Patients may need longer treatment to sustain protection, say the authors. We don't yet know how long.

The 274 participants were mostly British, aged 50-60 years, with a median body mass index of 33. They had a history of recurrent cellulitis, including an index recurrence no more than six months before recruitment. Participants with a body mass index over 33, lymphoedema, or at least three previous episodes had a significantly higher risk of treatment failure. They are the patients most likely to be prescribed long term prophylaxis, and they might need a higher dose, coupled with measures to reduce leg oedema.

N Engl J Med 2013;368:1695-703

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Viruses from ducks and chickens dominate the family tree of H7N9

The new avian influenza virus H7N9 is genetically diverse and evolved from at least four sources, including viruses carried by wild ducks, domestic ducks, and chickens, say researchers. The new virus's family tree suggests close links with an H7 virus isolated from ducks in Zhejiang province of China in 2011, and with another isolated from wild birds migrating along the east Asian flyway. This route crosses eastern China, South Korea, and Japan.

The N9 sequences may also have come from wild ducks that gather in large colonies for breeding during migration from southeast China along the same east Asian flyway, although European sequences also appear further up the family tree. Mallard, spot billed ducks, and teal form large mixed colonies with plenty of opportunities for genetic reassortment, say the

researchers. They also share habitat with China's domestic ducks.

The six internal genes of H7N9 probably evolved from H9N2 viruses isolated from diverse chicken populations, brought together through live transport, say the researchers. The final genetic reassortment probably took place during mixing of domestic ducks and chickens in Shanghai or adjacent provinces. H7N9 emerged around January and has already diversified into two different subclades, both highly pathogenic to humans. Ducks and chickens can carry the virus for long periods without symptoms.

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Azithromycin does not look cardiotoxic in a general population

Concerns were raised last year about a small excess of deaths from cardiovascular disease in US adults taking azithromycin, so Danish researchers looked for a similar signal using Denmark's comprehensive national databases. The results were reassuring. Current use of azithromycin was associated with no more cardiovascular deaths than current use of penicillin V in extensively adjusted analyses of more than eight million treatment episodes in adults aged 18-64 years (1.1 v 1.5 deaths/1000 person years; adjusted rate ratio 0.93, 95% CI 0.56 to 1.55). Those taking azithromycin had a higher risk of cardiovascular death than matching controls taking no antibiotics (2.85, 1.13 to 7.24), probably because acute infections raise risk, say the researchers. Azithromycin looks safe in a large general population of young and middle aged adults who might typically present for treatment to primary care services in a developed country.

The signal from the US emerged in a population who were eligible for federally funded health insurance (Medicaid). They had a substantially higher baseline risk of cardiovascular disease and death than the Danish participants. The two studies are complementary not contradictory, say the researchers. If there is a link between azithromycin and cardiovascular death, the absolute risk is small and confined to high risk adults.

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