3 Wilkinson SAJ, Richter A, Casey A, et al. Recurrent SARS-CoV-2 mutations in immunodeficient patients. *medRxiv* 2022; published online March 2. https://doi.org/10.1101/2022.03.02.22271697 (preprint).
4 Harvey WT, Carabelli AM, Jackson B, et al. SARS-CoV-2 variants, spike mutations and immune escape. *Nat Rev Microbiol* 2021; **19:** 409–24.
5 Rockett R, Basile K, Maddocks S, et al. Resistance mutations in SARS-CoV-2 delta variant after sotrovimab use. *N Engl J Med* 2022; **386:** 1477–79.

HPV vaccination and cervical cancer screening

Screening can cause harm (eg, anxiety, further tests, diagnostic labels, costs, morbidity, and death). Sometimes, a screening programme can bring net benefits when the Wilson and Jungner criteria are applied.[1] Screening can detect problems too early, leading to overdiagnosis and overtreatment, resulting in high financial costs, morbidity, and death. Screening healthy people should be considered a medical failure, a second-rate and burdensome approach, and at best should be a temporary, contingent stopgap between the real successes of prevention and cure. Screening (of healthy people) and early diagnosis (with speedy management of symptomatic patients) are ethically and scientifically distinct, but often wrongly elided.[2] The UK National Health Service, policy makers, and the general public need to understand that programmes should be continuously interrogated and dismantled as they become redundant to release funds for something more effective and to liberate people from the constant anxiety of routine check-ups and self-checking. The preliminary observational data about the effects of England's national human papillomavirus (HPV) vaccination programme from Milena Falcaro and colleagues' study[1] show that the programme has almost eliminated cervical cancer and precancer, albeit data only being available for women up to age 25 years.[3] The positive implications of changing the natural history of this disease were not anticipated or addressed.[3,4] It is inevitable that the death and morbidity trade-offs will change from benefits towards harms, especially given the known lifelong risks of prematurity in the offspring of women with surgically damaged cervices.[5] The criteria for the screening programme should be reviewed to determine if and when it should be offered to only those who have not had an HPV vaccination. Cervical cancer screening at the population level should not continue when previous harm to benefit weighings and justification have vanished.

SB is chair of HealthSense UK and declares no other competing interests.

Susan Bewley
susan.bewley@kcl.ac.uk

Department of Women and Children's Health, King's College London, London SE1 7NH, UK

1 UK National Screening Committee. Criteria for appraising the viability, effectiveness and appropriateness of a screening programme. Oct 23, 2015. https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme (accessed Dec 19, 2021).
2 NHS England and NHS Improvement. Screening and earlier diagnosis. https://www.england.nhs.uk/cancer/early-diagnosis/screening-and-earlier-diagnosis/ (accessed Dec 19, 2021).
3 Falcaro M, Castañon A, Ndlela B, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. *Lancet* 2021; **398:** 2084–92.
4 Cruickshank ME, Grigore M. Cervical cancers avoided by HPV immunisation. *Lancet* 2021; **398:** 2053–55.
5 Kyrgiou M, Athanasiou A, Kalliala IEJ, et al. Obstetric outcomes after conservative treatment for cervical intraepithelial lesions and early invasive disease. *Cochrane Database Syst Rev* 2017; **11:** CD012847.

Milena Falcaro and colleagues[1] reported that cervical cancer and grade 3 cervical intraepithelial neoplasia (CIN3) were prevented by a bivalent vaccine (Cervarix). The study showed that Cervarix was more effective against CIN3 than cervical cancer. Considering that human papillomavirus 16 (HPV16) and HPV18 account more for cervical cancer than CIN3, it is reasonable to assume that Cervarix prevents cervical cancer more than CIN3. In a 2007 phase 3 study, bivalent HPV vaccine showed high efficacy, preventing 90·4% of grade 2 CIN or worse.[2] Compared with cervical cancer, CIN3 is a heterogeneous disease that includes various stages of dysplasia,[3] and only 31·3% of cases progress into cancer within 30 years.[4] Since the introduction of regular inoculation of HPV immunisation, the risk of CIN3 progressing to cervical cancer would be mitigated. It is not surprising that pathologists might have paid less attention to missing the diagnosis of CIN3 compared with that of cervical cancer. These situations lead to underdiagnosis of CIN3, overestimating the effectiveness of HPV vaccination. We would like Falcaro and colleagues to make comments on this possibility.


Kazuhiro Nogi/AFP/Getty Images

MK is remunerated as Director of SBI Biotech and is an adviser of Mnes, unrelated to this Correspondence. EK received advisory fees from Otsuka Pharmaceutical, unrelated to this Correspondence. All other authors declare no competing interests.

**Sae Kamamoto, Anju Murayama, Tamae Hamaki, Eiji Kusumi, Masahiro Kami*
sae.joy1056210@gmail.com

Medical Governance Research Institute, Minato-ku, Tokyo 1087505, Japan (SK, AM, MK); Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan (SK); Tohoku University School of Medicine, Sendai, Miyagi, Japan (AM); Department of Internal Medicine, Navitas Clinic Shinjuku, Shinjuku, Tokyo, Japan (TH); Department of Internal Medicine, Navitas Clinic Tachikawa, Tachikawa, Tokyo, Japan (EK)

1 Falcaro M, Castañon A, Ndlela B, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. *Lancet* 2021; **398:** 2084–92.
2 Paavonen J, Jenkins D, Bosch FX, et al. Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. *Lancet* 2007; **369:** 2161–70.