

Increased incidence of cervical cancer in Sweden: an unlikely link with human papillomavirus (HPV) vaccination

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BACKGROUND

In 2017, the Centre for Cervical Cancer Prevention in Sweden (NKCx) reported an increase in the Swedish cervical cancer incidence from 9.7/100 000 in 2006–2009 to 11.5/100 000 in 2014–2015 with a p value of 0.03 (see the Swedish report's Table 9 on PDF page 49 of 87).¹

In April 2018, the *Indian Journal of Medical Ethics* (IJME) published a comment entitled 'Increased incidence of cervical cancer in Sweden: possible link with HPV vaccination'. In May 2018, the comment was retracted, because its author had used a pseudonym, which violated IJME's policy.² Sweden's human papillomavirus (HPV) vaccination programme was introduced in 2010, and the IJME comment author hypothesised that the increase in cervical cancer was possibly linked with HPV vaccination. Here, we argue why this is unlikely.

THE SWEDISH REPORT INCLUDED ONLY A MINORITY OF THE SWEDISH HPV VACCINEES

In 2010, Sweden initiated its HPV vaccination programme for girls aged 12 to 15 years. The Swedish report included data up until the end of 2015 for women aged 20 years and older.¹ Thus, very few of those who were included in the HPV vaccination programme were included in the Swedish report. In 2010, Sweden also conducted a catch-up vaccination programme for girls aged 15 to 18 years, who were 20 to 23 years old in 2015 and therefore included in the Swedish report.¹ However, nearly half (41%) of this catch-up cohort was not HPV vaccinated, and only 9% (269/2977) of the cervical cancers that occurred in Sweden from 2010 to 2015 occurred in women aged 20 to 24 years (see interactive database:³ '171 Livmoderhals (cervix uteri), oavsett

tumörtyp (cervix independent of tumour type)'; the peak incidence was in women aged 30 to 39 years). The relatively low HPV vaccination rate combined with low cervical cancer frequency in those aged 20 to 23 years are therefore unlikely to be the main contributors to the Swedish cervical cancer increase. The IJME comment author found that the increase in cervical cancer was most prominent in younger women and that the number of cases in the 20–49-year group increased from 202 cases in 2006 to 317 cases in 2015 – an increase of 50% – but the author did not investigate the catch-up cohort of those aged 20 to 23 years by itself.²

INCREASED IMMIGRATION FROM COUNTRIES WITH LIMITED CERVICAL SCREENING AND HPV VACCINATION

As of 2018, Sweden's population was about 10 million. Since 2010, Sweden has had a substantial increase in the number of immigrants.⁴ From 2012 to 2015, nearly 450 000 people immigrated to Sweden. Family reunion and asylum accounted for 64% of the immigration (about 285 000 individuals). Many immigrants came from countries with limited cervical cancer screening, no HPV vaccination and a high incidence of cervical cancer.⁵ Since female immigrants were enrolled in the Swedish cervical screening programme, the increased immigration could have contributed to the rise in cervical cancer incidence.

INCREASED SWEDISH FREQUENCY OF CERVICAL SCREENING LIKELY IDENTIFIED MORE CANCERS

Recently, Sweden had an increase in the frequency of cervical screening with a record high participation in 2015 (82% of eligible women).¹ The higher screening frequency



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may have increased the number of identified cervical cancers – especially of asymptomatic cancers and cancers in female immigrants that had limited or no previous cervical screening. Advances in cervical screening may also have contributed to cervical cancer identification; for example, the Swedish use of HPV testing as a cervical screening adjunct increased from nearly 10 000 tests in 2010 to more than 150 000 in 2015 (see the Swedish report's Figure 13 on PDF page 47 of 87).¹

NO COUNTRY OTHER THAN SWEDEN HAS REPORTED A SIMILAR CERVICAL CANCER INCREASE

To our knowledge, there have been no other regional or global reports that have reported a significantly increased cervical cancer incidence after the initiation of HPV vaccination programmes since 2006. For example, after the introduction of the HPV vaccines, the UK has had a stable cervical cancer incidence⁶ but the USA reported a significant decrease, indicating early effects of HPV vaccination.⁷ However, the UK's ethnic minorities had a higher incidence of cervical cancer and a lower HPV vaccine uptake compared with the rest of the population.⁸

SWEDEN HAD NO INCREASE OF OTHER HPV-RELATED CANCERS

Apart from cervical cancer, HPV is linked with anal, oropharyngeal, penile, vaginal and vulvar cancers (and non-cancerous diseases like genital warts and respiratory papillomatosis). The Swedish incidences of these other HPV-related cancers have been stable overall from 2005 to 2015, for example, anal cancer with 960 cases both in 2005 and 2015 and vaginal cancer with 46 cases in 2005 and 37 cases in 2015 (see interactive database:³ '1761 Vagina' and '154 Ändtarm och anus').

BIOLOGICAL IMPLAUSIBILITY

If the HPV vaccines contained HPV in an attenuated form, an increase in cervical cancer could have been biologically plausible. However, as the vaccines do not contain any HPV fragments – but only virus-like particles – it is unlikely that HPV vaccination could cause cervical cancer.

CONCLUSIONS

HPV vaccination has the potential to decrease HPV-related cancers. The increase in Swedish cervical cancer incidence is not likely to be caused by HPV vaccination. It may take several decades, however, before the HPV vaccines' effects on HPV-related cancers are fully known.

Correction notice Since this paper was first published online, Peter Gøtzsche's affiliation has been updated to the Institute for Scientific Freedom.

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Competing interests PCG spoke by video link about the HPV vaccines at the IFICA conference in 2018 but received no fee or reimbursement for this. PCG and TJ were co-signatories of a complaint to the European Ombudsman on maladministration in relation to the EMA investigation of possible harms from HPV vaccines. PCG does not regard this as a competing interest. TJ was a co-recipient of a UK National Institute for Health Research grant (HTA – 10/80/01 Update and amalgamation of two Cochrane Reviews: neuraminidase inhibitors for preventing and treating influenza in healthy adults and children –https://www.journalslibrary.nihr.ac.uk/programmes/hta/108001#). TJ is also in receipt of a Cochrane Methods Innovations Fund grant to develop guidance on the use of regulatory data in Cochrane reviews. TJ is occasionally interviewed by market research companies about phase I or II pharmaceutical products. In 2011–2014, TJ acted as an expert witness in a litigation case related to the antiviral oseltamivir, in two litigation cases on potential vaccine-related damage, and in a labour case on influenza vaccines in healthcare workers in Canada. He has acted as a consultant for Roche (1997–1999), GSK (2001–2002), Sanofi-Synthelabo (2003) and IMS Health (2013). In 2014–2016, TJ was a member of three advisory boards for Boehringer Ingelheim. TJ was a member of an independent data monitoring committee for a Sanofi Pasteur clinical trial on an influenza vaccine. A full disclosure is here <https://restoringtrials.org/competing-interests-tom-jefferson/>

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