

## **Early detection strategies urgently needed to limit HPV-associated OPSCC**

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We read with interest the recent letter by Prue *et al*<sup>1</sup> stating the need for urgent introduction of gender neutral HPV vaccination in the UK. While we agree with their economic analysis of the current situation, we would also like to draw attention to the potential future costs to UK society in general.

In July 2018, the UK government announced the extension of the UK Human Papillomavirus (HPV) vaccination programme to include boys as well as girls, following the recommendation by the Joint Committee on Vaccination and Immunization (JCVI). General practitioners and pediatricians have been informed and the hope is that the overall uptake will be as good as achieved in girls. This is considered a significant advance in the fight against HPV-associated oropharyngeal cancer which has one of the most rapidly rising incidences of any cancer in high-income countries and is primarily a disease of men. Male rates of oropharyngeal squamous cell cancer (OPSCC) have overtaken cervical cancer in the UK for the first time in 2016 (Lechner *et al*/2019), a similar trend observed in the US in 2012. Assuming vaccination coverage remains good, the effects of the vaccination programme will cause a significant drop of the rates of HPV-associated oropharyngeal cancer in current and future vaccination cohorts of boys and girls, but only in decades to come. Until this time, the rates of oropharyngeal cancer are still predicted to rise significantly.

The incidence of oropharyngeal cancers in the UK was more than 3 times higher in men than in women in 2016 (9.9 male cases per 100,000 per year vs. 3.2 female cases) and in the US more than 6 times higher than in women in 2014 (7.8 male cases per 100,000 per year vs. 1.3 female cases). Rates of OPSCC are anticipated to fall in women before it does in men due to the introduction of female HPV vaccination in 2008

that has achieved good overall coverage, though ongoing adherence to vaccination will be required for the reduction in incidence to be maintained.

Figure 1 shows the OPSCC estimates for the next 25 years (cases per 100,000, men). The predicted rate is based on a linear regression model based on data for the 2011-2016 period (supplemental material). After 2040-2050 OPSCC cases per 100,000 are likely to drop due to the ongoing vaccination campaign, although this reduction may only be modest if the adherence to vaccination is low. Predicted rates for the year 2040 indicate an expected number of over 25 male cases per 100,000.

The above rates were used in the following section to estimate the cost of oropharyngeal cancer treatment in the UK. Apart from the human cost (disease and death), it is estimated that oropharyngeal cancer treatment has cost the NHS in England alone an estimated £115 million over 5 years (from 2006-2011) with around 75% of treatment costs spent on men who have higher mortality rates than women<sup>2</sup>. Costs have increased year on year from £17.2 million in 2006 to £30.3 million per year in 2011. The costs are likely to be much higher today, not only because of the rapidly increasing rates, but also because of rising costs of cancer treatments. Based on the above increase of incidence rates of OPSCC, the treatment cost estimates and the population estimates, we have calculated the overall costs for OPSCC treatment in the UK from 2019-2038 for men only. The calculated undiscounted estimate is in excess of £2Bn.

Furthermore, it is important not to overlook the broader societal costs of OPSCC due to lost workplace productivity. While there has been no detailed analysis of the productivity costs of OPSCC in the UK, a recent assessment of productivity lost to head and neck cancers in Ireland estimate a cost per case diagnosed (within the working age population) equivalent to approximately £235,000<sup>3</sup>. Applying that cost to

the current incidence of oropharyngeal cancers in England in 2016 under age 65 (ICD-O-3: C01, C05, C09 and C10; Supplemental methods) yields an overall cost of £531 million per year when adjusted to the overall size of the UK population<sup>4</sup>. This broader societal cost will amount an undiscounted total of in excess of £18Bn in the UK from 2019-2039 for men only.

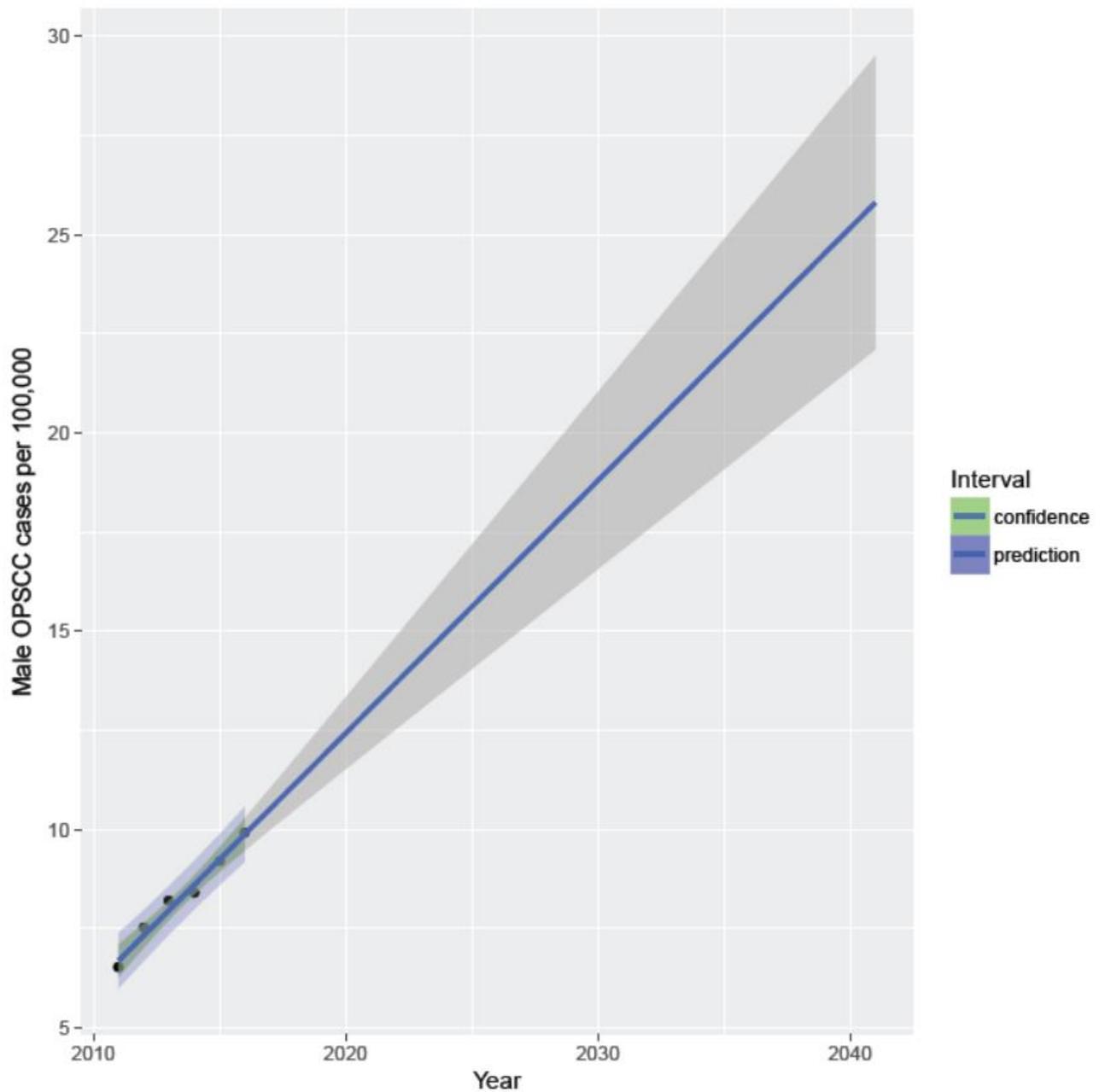
In summary, male rates of OPSCC have overtaken cervical cancer in the UK for the first time in 2016, a similar trend observed in the US in 2012. As demonstrated above, male rates of OPSCC are predicted to rise significantly in the next 20-30 years and associated OPSCC treatment costs for men alone are estimated to be in excess of £2Bn in the UK and wider societal costs in excess of £18Bn in the next 20 years. Hence, at this current stage, it is of utmost importance to support the development of effective early detection strategies for both persistent, oncogenic HPV infection and HPV-associated oropharyngeal cancer that may allow curative treatment of precancerous stages as seen in cervical cancer. This will be the only way to substantially decrease the significant disease burden that is expected until gender-neutral vaccination becomes fully effective in decades to come. Without such urgency, British men and women can expect avoidable and unnecessary future cancer deaths.

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### **References**

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**Figure 1:** OPSCC estimates for the next 25 years (cases per 100,000, men). The blue line indicates the predicted rate according to a linear regression model based on data for the 2011-2016 period (UK Office for National Statistics; supplemental material). The grey area indicates the 95% confidence interval for this prediction. After 2041 OPSCC cases per 100,000 are likely to drop due to the ongoing vaccination campaign, although this drop could be low if the campaign secures a limited response. Predicted rates for the year 2041 indicate an expected number of over 25 cases per 100,000 (25.80, 95% CI: 22.05-29.55).