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Is the recent increase in cervical cancer in women aged 20–24 years in England a cause for concern?

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ABSTRACT

The rates of cervical cancer (CxCa) in England among women aged 20–24 yrs increased from 2.7 in 2012 to 4.6 per 100,000 in 2014 ($p = 0.0006$). There was concern that the sudden increase was linked to the withdrawal of cervical screening in women aged 20–24 (a policy that affected women born since 1984).

We analyse granular data on age and FIGO stage at diagnosis using a generalised linear model to see whether the unprecedented increase in CxCa in young women in 2014 was linked to the change in 2012 to the age at which the first invitation to screening was sent (from 25.0 to 24.5).

Annual rates of CxCa per 100,000 women aged 20.0–24.5 yrs decreased gradually over time, whereas at age 24.5–25.0 yrs they increased from an average of 16 pre-2013 to 49 in 2015. An increase of 20.3 per 100,000 women aged 24.5–25.0 yrs (95% CI: 15.2–25.4) was associated with inviting women for screening at age 24.5 yrs instead of at age 25.0. At age 25.0–25.5 yrs, rates decreased by 23.7 per 100,000 after women were invited at age 24.5 yrs ($p < 0.001$). All these changes were limited to stage I CxCa. There was a dramatic increase in diagnoses at age 25 yrs in 2009–2011 associated with changing the age at first invitation from 20 yrs to 25 yrs. No changes were observed at age 26.0–27.0 yrs.

The increase in CxCa aged 20–24 is attributable to an increase in the proportion of women first screened aged 24.5 yrs. The increase was limited to stage I CxCa. There is no evidence of a lack of screening leading to increasing rates.

1. Introduction

In 2004 the age of first cervical screening invitation in England was increased from 20 to 25 (Public Health England). This reflected a major change in screening policy and was based on evidence that screening at ages 20–24 provided no population benefit in terms of cancer prevention (Sasieni et al., 2003). In 2012, the age of sending out the first screening invitation was changed again; this time to 24.5 years. This was simply to enable women to be screened by their 25th birthday as it was noted that many women were only screened following a second reminder up to 6 months after the initial invitation (Health and Social Care Information Centre, 2013); it was not considered to be a major policy change. Approximately 62% of women aged 25–29 attend screening (Health and Social Care Information Centre, 2013). Amidst these changes HPV vaccination was introduced in 2008 for girls aged 12–13 with catch-up for those aged 14–18. Many people expected CxCa rates in women aged 20–24 to fall by 2014 as the vaccinated cohorts entered their twenties. However, in 2016 national statistics showed a worrying and substantial increase in the rate of cervical cancer (CxCa) at ages 20 to 24 (from 2.7 in 2012 to 4.6 per 100,000 in 2014, $p = 0.006$) (Office for National Statistics, 2016). Rates in this age group had been stable until 2012. Rates of CxCa in England at ages 25–29 have been steadily increasing from around the time of the first policy change onwards (from 10 per 100,000 in 2003 to over 20 per 100,000 in 2014).

The sudden increase in CxCa in women aged 20–24 sparked concerns that by withdrawing screening in 20–24 year olds, an epidemic stemming from lack of prevention was starting to emerge. This was particularly concerning as some argued that the lack of a reduction in rates showed that HPV immunisation had been ineffective. This paper describes an evaluation that was undertaken in response to these concerns. The analysis explores trends in CxCa in women aged < 30 yrs between 2006 and 2015, focussing on changes in the age at diagnosis and FIGO stage, over time. The aim was to elucidate what factors are driving the increase in cervical cancer among women aged 20–24 using routinely collected incidence data.

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2. Methods

Notational convention: when we state the age in years without a decimal such as 26 we mean ≥ 26 and < 27. When we use an age range including a decimal we mean ≥ to the lower age and < the upper age. Thus "20–24" is the same as "20.0–25.0".

2.1. Data

We plotted trends based on routinely published Cancer Registration Statistics for England from 1990 to 2015 (Office for National Statistics, 1990–2015); for Scotland from 1990 to 2014 from the Scottish Cancer Registry (Information Services Division. NHS National Services, 2016); for Wales data between 1990 and 2011 from the Welsh Cancer Intelligence and Surveillance Unit (The Welsh Cancer Intelligence and Surveillance Unit, 2013) and for cancers diagnosed between 2012 and 2015 from the Welsh Cancer Intelligence and Surveillance Unit website (Welsh Cancer Intelligence and Surveillance Unit, 2016). To ascertain the number of women invited for their first screening test at ages 20–24 we used data from Table 4 of the KC53 Part B returns published in the NHS Cervical Screening Programme Statistics, Source: KC53, Table 4 from 2010/11 to 2014/15 (Health and Social Care Information Centre and Screening and Immunisations, 2016).

In addition, by special request, we obtained (from the National Cancer Registration and Analysis Service, Public Health England) diagnoses of CxCa (ICD10 C53) in England by FIGO stage at diagnosis for ages 20–29 with detailed breakdown of those occurring at age 24.5–25.0, 25.0–25.5 and those at 25.5–26.0 for 2006 to 2015. These age ranges were chosen to examine in detail the effect of sending screening invitations six months earlier (i.e. at age 24.5 instead of at age 25.0).

It should be noted that the date of diagnosis recorded by the cancer registry should be the date on which the biopsy providing histological confirmation of the cancer was taken. HPV triage was introduced into cervical screening in England in 2012–2013. Prior to that a borderline (ASCUS) or mild (LSIL) smear would have been repeated at 6 months and women were only discharged from 6-monthly testing after three consecutive normal smears. Thus it could be 18 months or more from a screening abnormality until referral for colposcopy and cancer diagnosis. With HPV triage women should either be referred to colposcopy or returned to routine screening following their screen. National policy is for women to be informed of their results of screening within 2 weeks; in 2014–15 about 90% met the target (fewer than 1% took over 3 weeks) (Health and Social Care Information Centre, 2015). Time from referral to colposcopy appointment varied depending on the severity of cytology: 98% of high-grade cytology was offered an appointment within 4 weeks, but it took 8 weeks to include 98% of all referrals. Some clinics treat women with high-grade cytology at first colposcopy appointment, but most recall those with high-grade disease on biopsy for subsequent treatment. National data show that 82% all screen-detected cancers are diagnosed within four months of the screening test that led to colposcopy referral (Sasieni and Castanon, 2014).

2.2. Assumptions

The change in policy from first inviting women from age 20 to age 25 years was implemented in England over a 15-month period starting in August 2004. Since we did not have the date at which an individual was first invited for cervical screening, it is not clear whether women born between 26 August 1984 and 3 November 1985 were invited for screening before age 25. We estimate year of birth using year of diagnosis minus age (in years) at diagnosis. We categorised all women born before 1984 as 'invited from age 20', those born between 1986 and 1988 as 'invited from age 25'. The change in policy inviting women at age 25.5 was implemented in December 2012 therefore we categorise women born from 1989 onwards as 'invited from age 24.5'. Women born in 1984 and 1985 were labelled 'mixed group' because they may have either been invited from 20 or from 25 years.

We grouped FIGO stage as follows: Stage IA, Stage IB and Stage II or worse. Since some women had a recorded FIGO stage of I without further detail we proportionally distributed these cases between FIGO IA and FIGO IB. Those women with an unknown FIGO stage at diagnosis were distributed proportionally between stages IB and II or worse. We assume that those with missing stage were not stage IA because we know from previous research using the Audit of Invasive Cancer (Sasieni and Castanon, 2014) that women included in the Audit with un-staged cancers who eventually have their cancers staged rarely had stage IA cancer. We also performed a sensitivity analysis excluding cases of unknown FIGO stage.

2.3. Statistics

Cancer rates by nation (England, Scotland, Wales) and five-year age were smoothed against year of diagnosis using symmetric nearest neighbour smoothing (using the 'running' command in STATA).

An age-period-cohort analysis was not considered because i) we have little follow up for women invited from age 24.5, ii) we did not have number of cancers in six monthly intervals for all age groups and iii) not all cohorts reached age 30 by 2015. Instead a backward stepwise generalised linear model using the Poisson family and identity link function was fitted to obtain the change in rates associated with the age at screening invitation.

We include the following covariates in the regression: i) year of diagnosis; ii) a dummy variable (1/0) to indicate diagnoses in 2009, corresponding to the year in which reality TV star Jade Goody died. There were about half a million extra attendances to screening in England between her diagnosis (August 2008) and death (March 2009). At its peak, in March 2009 attendance was 70% higher than usual (Lancucki et al., 2012); iii) a variable to reflect the proportion of the birth cohort affected by the policy to screen from age 25.0 ($X_{25} = 0$ for birth cohorts < 1984, = 0.35 for 1984, = 0.70 for 1985 and = 1 for all other cohorts); iv) a variable to reflect the proportion of the birth cohort first invited for screening at age 24.5 ($X_{24} = 0$ for birth cohorts < 1989, = 0.75 for the 1989 cohort and = 1 for all other cohorts). Note that no woman has both $X_{24} = 1$ and $X_{25} = 0$. Sensitivity analyses on the effect of changing the proportion of women invited for screening in the 'mixed' cohorts were carried out. For the comparison of stage at diagnosis pre and post change in age at invitation we used a chi-square statistic with two degrees of freedom. p values of < 0.05 were considered statistically significant.

Data analyses were performed in STATA 13.1 (StataCorp. 1985–2013. Stata Statistical Software: Release 13.1. College Station, TX, USA: StataCorp LP).

3. Results

3.1. Comparison between countries with different policies

Comparison of incidence rates in England (where screening women aged 20–24 yrs was phased out between 2004 and 2009) with rates in Scotland and Wales (where screening from age 20 yrs continued until after 2014) are presented in Fig. 1. Year-to-year variation in rates is much greater in Scotland and Wales than in England reflecting the very different population sizes.

In England an increase in rates among 20–24 year old women is evident from 2013 onwards. This coincides with an increase in the number of women under age 25 invited for screening for the first time (reflecting the change in policy to send out invitation 6 months earlier) from 35,435 invitations in 2010–11 to 189,544 in 2014–15, Table 1. Cervical cancer rates for women aged 20–24 yrs in Scotland and Wales have also increased over the last 10 years, Fig. 1. In fact, rates in