Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data

Hammad Ali,[1] Basil Donovan,[1 2] Handan Wand,[1] Tim R H Read,[3 4] David G Regan,[1] Andrew E Grulich,[1] Christopher K Fairley,[3 4] Rebecca J Guy[1]

EDITORIAL by Barton and O'Mahony

[1]The Kirby Institute, University of New South Wales, Sydney, NSW 2052, Australia
[2]Sydney Sexual Health Centre, Sydney Hospital, Sydney, NSW 2000, Australia
[3]Melbourne Sexual Health Centre, Carlton, VIC 3053, Australia
[4]School of Population Health, University of Melbourne, Parkville, VIC 3010, Australia
Correspondence to: B Donovan
bdonovan@kirby.unsw.edu.au

Cite this as: *BMJ* 2013;346:f2032
doi: 10.1136/bmj.f2032

This is a summary of a paper that was published on bmj.com as *BMJ* 2013;346:f2032

bmj.com/podcasts
Listen to a podcast discussion with the authors of this paper at bmj.com/multimedia

STUDY QUESTION

What is the population effect on genital warts of the quadrivalent national human papillomavirus vaccination programme that started in Australia in 2007?

SUMMARY ANSWER

Significant declines in the proportion of young women with genital warts and the absence of genital warts in vaccinated women in 2011 suggest that the vaccine has high efficacy outside of the trial setting; large declines in diagnoses of genital warts in heterosexual men are probably due to herd immunity.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The quadrivalent human papillomavirus vaccine offers up to 100% protection against lesions caused by human papillomavirus 6 and 11, and declines in the incidence of genital warts have been documented in several countries, depending on the level of vaccine coverage. In women, with a 83% first dose vaccine coverage, a 93% decline in diagnosis of genital warts was seen by the fifth year of the national quadrivalent human papillomavirus vaccination programme in Australia, and no women who reported that they had been vaccinated were found to have genital warts in the final year of the study.

Participants and setting

Between 2004 and 2011, 85 770 Australian born patients were seen for the first time at eight sexual health services in Australia, and 7686 (9.0%) were diagnosed as having genital warts. The two largest clinics also collected self reported human papillomavirus vaccination status from 2009.

Design

This was a trend analysis of national surveillance data.

Primary outcome(s)

Using rate ratios, we compared trends in the proportion of new patients diagnosed as having genital warts in the pre-vaccination period (2004 to mid-2007) and the vaccination period (mid-2007 to the end of 2011).

Main results and the role of chance

Significant declines occurred in the proportions of under 21 year old (92.6%) and 21-30 year old (72.6%) women diagnosed as having genital warts in the vaccination period—from 11.5% in 2007 to 0.85% in 2011 (P<0.001) and from 11.3% in 2007 to 3.1% in 2011 (P<0.001), respectively. No significant decline in genital wart diagnoses occurred in women aged over 30. We saw significant declines in the proportions of under 21 year old (81.8%) and 21-30 year old (51.1%) heterosexual men diagnosed as having genital warts in the vaccination period—from 12.1% in 2007 to 2.2% in 2011 (P<0.001) and from 18.2% in 2007 to 8.9% in 2011 (P<0.001), respectively. No significant decline in genital wart diagnoses occurred in men aged over 30. In 2011 no diagnoses of genital warts were made among 235 women under 21 years of age who reported previous human papillomavirus vaccination.

Proportion of Australian born women diagnosed as having genital warts at first visit, by age group, 2004-11

Bias, confounding, and other reasons for caution

The main limitation of this study is that sexual health services target populations that are at higher risk of sexually transmissible infections, introducing a bias towards a higher prevalence of genital warts. As the study was clinic based, a change in the profile of patients seen over the study period is possible. However, the prevalence of chlamydia increased whereas that of genital warts decreased.

Generalisability to other populations

Both clinic based and population based methods have shown declines in genital warts in other countries. Differences in the degree of decline are attributable to varying rates of coverage with the vaccine.

Study funding/potential competing interests

CSL Biotherapies funded the surveillance network. CKF owns shares in CSL Biotherapies. CKF, AEG, DGR, RJG, and BD have received honorariums or research funding from CSL Biotherapies, Sanofi Pasteur MSD, and/or Merck. AEG sits on the Australian advisory board for the Gardasil vaccine. TRHR is a site investigator for a Merck human papillomavirus vaccine study.

Strategy for detection of prostate cancer based on relation between prostate specific antigen at age 40-55 and long term risk of metastasis: case-control study

Andrew J Vickers,[1] David Ulmert,[2 3] Daniel D Sjoberg,[1] Caroline J Bennette,[4] Thomas Björk,[3] Axel Gerdtsson,[3] Jonas Manjer,[5] Peter M Nilsson,[6] Anders Dahlin,[7] Anders Bjartell,[3] Peter T Scardino,[2] Hans Lilja[2 8 9 10 11]

[1]Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, USA
[2]Department of Surgery (Urology), Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, USA
[3]Department of Urology, Lund University, Skåne University Hospital, Malmö, Sweden
[4]Pharmaceutical Outcomes Research and Policy Program University of Washington, Box 357630, H375 Health Science Building, Seattle, WA 98195-7630, USA
[5]Department of Surgery, Lund University, Skåne University Hospital, Malmö, Sweden
[6]Department of Medicine, Lund University, Skåne University Hospital, Malmö, Sweden
[7]Department of Clinical Microbiology, Lund University, Skåne University Hospital, Malmö, Sweden
[8]Department of Laboratory Medicine, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, USA
[9]Department of Medicine (GU-Oncology), Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, USA
[10]Department of Laboratory Medicine and Clinical Sciences in Malmö, Lund University, Skåne University Hospital, Malmö, Sweden
[11]Nuffield Department of Surgical Sciences, University of Oxford, John Radcliffe Hospital, Oxford, UK
Correspondence to: H Lilja, Memorial Sloan-Kettering Cancer Center, 1275 York Ave (Box 213), New York, NY 10065, USA
liljah@mskcc.org

Cite this as: *BMJ* 2013;346:f2023
doi: 10.1136/bmj.f2023

This is a summary of a paper that was published on bmj.com as *BMJ* 2013;346:f2023

bmj.com

- Research: Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen (*BMJ* 2012;344:d7894)
- Clinical review: Prostate cancer screening and the management of clinically localized disease (*BMJ* 2013;346:f325)

STUDY QUESTION

What is the association between prostate specific antigen (PSA) concentration at age 40-55 and subsequent risk of prostate cancer metastasis and mortality in an unscreened population, when should screening start, and can rescreening be risk stratified?

SUMMARY ANSWER

Baseline PSA concentration is associated with long term risk of prostate cancer metastasis and death.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

PSA screening can reduce the risk of death from prostate cancer because of early diagnosis and treatment. The balance remains uncertain between these benefits versus harms associated with overdiagnosis and overtreatment. Measurement of PSA concentration in early midlife can identify a small group of men at increased risk of prostate cancer metastasis several decades later and these men should undergo careful surveillance. Three lifetime screenings (mid to late 40s, early 50s, and 60) are probably sufficient for at least half of men.

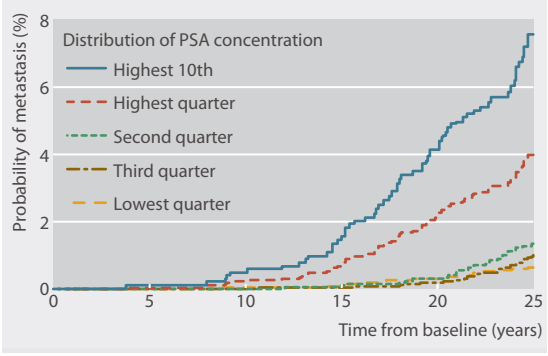
Participants and setting

The cohort consisted of Swedish men aged 27-52 who provided a blood sample at baseline in 1974-84, of whom a subgroup provided a second sample six years later. Rates of PSA testing remained low during extended follow-up.

Design, size, and duration

The study design was a case-control study nested with in a cohort of 21 277 men, of whom 4922 gave a second sample. Median follow-up was 27 years. PSA was measured in archived blood plasma samples. Metastasis or death from prostate cancer was ascertained by review of case notes.

Cumulative incidence of evidence of metastasis or death from prostate cancer by PSA concentration at age 45-49



Main results and the role of chance

The risk of prostate cancer death was associated with baseline PSA: 44% of deaths (95% confidence interval 34% to 53%) occurred in men with concentrations in the highest 10th of the distribution at age 45-49 (≥1.6 µg/L) with a similar proportion for the highest 10th at age 51-55 (≥2.4 µg/L; 44%, 32% to 56%). Although a 25-30 year risk of prostate cancer metastasis could not be ruled out by concentrations below the median at age 45-49 (0.68 µg/L) or 51-55 (0.85 µg/L), the 15 year risk remained low at 0.09% (0.03% to 0.23%) at age 45-49 and 0.28% (0.11% to 0.66%) at age 51-55, suggesting longer intervals between screening would be possible in this group. The risk of prostate cancer metastases by 15 year follow-up was low even for men in the highest 10th of concentrations at age 40 (≥1.3 µg/L; 0.6%). It seems likely that few tumours become incurable between the ages of 40 and 45, and it is therefore difficult to justify initiating PSA screening at age 40 for men with no other relevant risk factor. Given existing data on the risk of death by PSA concentration at age 60, these results suggest that three lifetime tests for PSA (mid to late 40s, early 50s, and 60) should be sufficient to rule out lethal cancer for half of men.

Bias, confounding, and other reasons for caution

There is little room for bias or confounding given a highly representative cohort subject to low rates of PSA testing during extended follow-up.

Generalisability to other populations

Although the study population was predominantly white, previous research has suggested no large racial differences with respect to the relation between PSA concentration and risk of prostate cancer. Absolute risks of death from prostate cancer might be lower in contemporary populations because of improved and more aggressive treatment. This would not importantly affect the relative risks between different PSA strata.

Study funding/potential competing interests

Funding support was provided from the National Cancer Institute, Swedish Cancer Society, the Sidney Kimmel Center for Prostate and Urologic Cancers, David H Koch through the Prostate Cancer Foundation, the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre Fundación Federico, and MSKCC PCPR (Prevention Control and Population Research Program) Goldstein. Three of the authors hold patents for methods to predict the result of prostate biopsy.

Parental depression, maternal antidepressant use during pregnancy, and risk of autism spectrum disorders: population based case-control study

Dheeraj Rai,[1 2 3] Brian K Lee,[4] Christina Dalman,[2] Jean Golding,[5] Glyn Lewis,[1] Cecilia Magnusson[2]

[1]Centre for Mental Health, Addiction and Suicide Research, School of Social and Community Medicine, University of Bristol, Bristol BS8 2BN, UK
[2]Division of Public Health Epidemiology, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden
[3]Avon and Wiltshire Partnership Mental Health NHS Trust, Bristol, UK
[4]Department of Epidemiology and Biostatistics, Drexel University School of Public Health, Philadelphia, PA, USA
[5]Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, UK
Correspondence to: D Rai **dheeraj.rai@bristol.ac.uk**

Cite this as: *BMJ* 2013;346:f2059
doi: 10.1136/bmj.f2059

This is a summary of a paper that was published on bmj.com as *BMJ* 2013;346:f2059

bmj.com
- Practice: Depression during pregnancy (*BMJ* 2007;334:1003)
- Clinical review: Diagnosis and management of autism in childhood (*BMJ* 2011;343:d6238)

STUDY QUESTION

Is parental depression or maternal antidepressant use during pregnancy associated with a higher risk of autism spectrum disorders in offspring?

SUMMARY ANSWER

Offspring with a prenatal history of maternal depression were at a higher risk of autism spectrum disorder, particularly autism without intellectual disability. This association was strongest in children of women reporting antidepressant use at the first antenatal interview, and was present for selective serotonin reuptake inhibitors (SSRIs) as well other monoamine reuptake inhibitors.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

It is still unclear whether parental depression is causally associated with autism spectrum disorders, and recently an association between in utero exposure to SSRIs and autism in offspring was reported. This study found evidence for an association between maternal but not paternal depression and autism spectrum disorders in offspring. It replicates the association between antidepressant use during pregnancy and autism, but highlights that SSRIs as well as non-selective monoamine reuptake inhibitors may be implicated, and that the associations appear specific to autism without intellectual disability.

Design, setting, and participants

This case-control study was nested within a register based cohort of young people aged 0-17 years living in Stockholm County, Sweden between 2001 and 2007 (n=589 114). There were 4429 cases of autism spectrum disorder (1828 with intellectual disability and 2601 without), and 43 277 age and sex matched controls in the parental depression analysis; of these 1679 autism cases and 16 845 controls had information on maternal antidepressant use during pregnancy.

Outcomes and exposure variables

Outcomes were an autism spectrum disorder diagnosis, with or without intellectual disability, identified using multisource case ascertainment. Exposures were a registered secondary care diagnosis of maternal and paternal depression before the birth of the child; and maternal antidepressant use during pregnancy, recorded at the first antenatal interview (available only for children born from 1995 onwards). Potential confounders included other recorded psychiatric disorders, birth parity; and parental ages, migration status, income, education, and occupation.

Main results and the role of chance

A history of maternal depression (adjusted odds ratio 1.49, 95% confidence interval 1.08 to 2.08) but not paternal depression was associated with an increased risk of autism spectrum disorders in offspring. In the subsample with medication data, this association was confined to women reporting antidepressant use during pregnancy (3.34 1.50 to 7.47, P=0.003), irrespective of whether use of SSRIs or non-selective monoamine reuptake inhibitors was reported. All associations were higher for children with autism without intellectual disability, with no evidence of an increase in risk for those with intellectual disability. Assuming an unconfounded, causal association, antidepressant use during pregnancy explained 0.6% of autism spectrum disorder cases.

Bias, confounding, and other reasons for caution

Confounding by indication is a concern since the associations for antidepressant use during pregnancy may reflect an association between severe depression during pregnancy and autism spectrum disorder. Parental depression was based on secondary care data and therefore underascertained.

Generalisability

The results of this large population based study are generalisable to Sweden and consistent with those recently reported in a US study.

Study funding/potential competing interests

This work was funded by the Swedish Research Council, Stockholm County Council, Swedish Council for Working Life and Social Research, and Swedish Regional ALF grants. The funders had no role in the conduct or reporting of the research.

Conditional logistic regression analysis showing relation between maternal depression, antidepressant use during pregnancy, and autism spectrum disorder in offspring (with and without intellectual disability) in children born between 1995 and 2003

	Adjusted odds ratio* (95% CI)		
Variables	Autism spectrum disorder	Autism spectrum disorder with intellectual disability	Autism spectrum disorder without intellectual disability
No antidepressant use:			
No depression	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Depression	1.06 (0.68 to 1.66)	1.06 (0.54 to 2.07)	1.04 (0.57 to 1.92)
Antidepressant use:			
Depression	3.34 (1.50 to 7.47)	1.81 (0.39 to 8.56)	4.94 (1.85 to 13.23)
No depression	1.61 (0.85 to 3.06)	0.93 (0.27 to 3.21)	2.10 (0.97 to 4.57)

*Adjusted for history of psychiatric disorders other than depression, parental ages, income, education, occupation, migration status, and parity.

Persistent pain and sensory disturbances after treatment for breast cancer: six year nationwide follow-up study

Mathias Kvist Mejdahl,[1] Kenneth Geving Andersen,[1] Rune Gärtner,[2] Niels Kroman,[2] Henrik Kehlet[1]

[1]Section for Surgical Pathophysiology, 7621, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen, Denmark
[2]Department of Breast Surgery, 3104, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
Correspondence to: M K Mejdahl **mathias.kvist.mejdahl@rh.regionh.dk**, K G Andersen **kenneth.geving.andersen@rh.regionh.dk**

Cite this as: *BMJ* 2013;346:f1865
doi: 10.1136/bmj.f1865

This is a summary of a paper that was published on bmj.com as *BMJ* 2013;346:f1865

MKM and KGA contributed equally to this work

bmj.com

- Research: Priorities for women with lymphoedema after treatment for breast cancer (*BMJ* 2011;342:d3442)
- Research: Comparing hospital and telephone follow-up after treatment for breast cancer (*BMJ* 2009;338:a3147)

STUDY QUESTION

What is the long term development in prevalence and severity of persistent pain and sensory disturbances in women after treatment for primary breast cancer?

SUMMARY ANSWER

Persistent pain and sensory disturbances remain a problem five to seven years after treatment for breast cancer but seem to fluctuate considerably over time. Young age and axillary dissection are risk factors for long term pain and sensory disturbances.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

About 25-60% of women experience persistent pain after treatment for breast cancer. This study shows that it is not a static problem. Five to seven years after treatment, a third of women who reported pain two years after treatment no longer reported pain, and 15% of women without pain two years after treatment reported pain four years later.

Participants and setting

3253 women treated for primary breast cancer in 2005 and 2006 participated in a nationwide questionnaire study in 2008 to examine the prevalence of persistent pain after treatment for breast cancer and sensory disturbances. This study followed up the same cohort in 2012, when 2828 women were eligible. Of these, 108 were subsequently excluded, and 2411 (89%) women participated in this study.

Design

Repeated cross sectional study of all women in the Danish Breast Cancer Cooperative Group database who were treated for primary breast cancer in 2005 and 2006, but had no recurrent or other cancer, reconstructive breast surgery, bilateral surgery, emigration, or death. The questionnaire used was identical to the one used in the 2008 study.

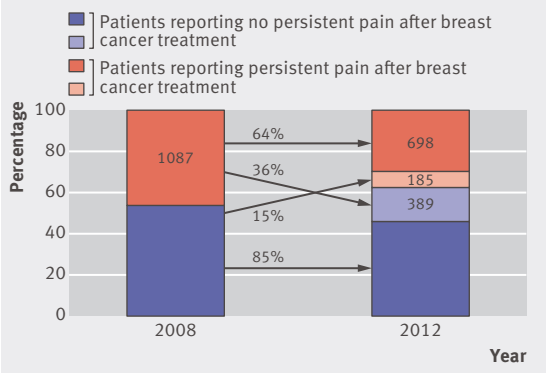
Primary outcome

The primary outcome was the prevalence of persistent pain five to seven years after treatment for breast cancer divided into well defined treatment groups. Persistent pain was defined as the presence of pain in the breast area, side of the body, axilla, or arm on the operated side. We also compared pain with the results from the previous 2008 study.

Main results and the role of chance

The prevalence of persistent pain after treatment for breast cancer was 22-53%, depending on treatment. For 2012 compared with 2008, 37% (903) versus 45% (1090) reported pain and 16% (378) versus 19% (463) reported pain ≥4 on a numerical rating scale (0-10) at least on a weekly basis. Risk factors for persistent pain after treatment were axillary lymph node dissection compared with sentinel lymph node biopsy and young age. At follow-up, 36% (389) of women who reported pain in 2008 were pain free in 2012, and 15% (185) who were pain free in 2008 reported pain in 2012. No particular method of treatment or age was associated with a pain increase from 2008 to 2012.

Development of persistent pain from 2008 to 2012 after treatment for breast cancer



Bias, confounding, and other reasons for caution

Between the 2008 study and this study, 533 women were excluded and a further 309 did not respond to the questionnaire, which could introduce selection bias. Nevertheless, this study reflects the majority of women who have undergone treatment for breast cancer, while those excluded represent specific problems all of which can have different influences on problems related to pain. The response rate was high, minimising the potential selection bias. Smoking, psychosocial factors, and other comorbidities were not recorded and could introduce confounding.

Generalisability to other populations

This study was conducted on a nationwide Danish cohort, which is relatively ethnically homogenous and benefits from a uniform public healthcare system. The results might therefore not necessarily be applicable to other ethnic groups or healthcare systems.

Study funding

This study was partially funded by a grant from the Danish Cancer Society and the Innovative Medicines Initiative Joint Undertaking, under EU grant agreement No 115007.