P-04-640 Bring Down the Age of Smears to 18 - Correspondence from the National Screening Committee to the Chair, 13.08.15

For the attention of William Powell

Dear Mr Powell,

I enclose the UK National Screening Committee response to the petitions P-04-640 to bring down the age of cervical smear screening to 18.

Please note that we intend to send a hard copy of this response by post, including all the supporting documents. Could you please provide me with the most appropriate postal address in which to send by post to the petitions team.

Note, also that the letter has been scanned in and originally contained three electronic links to information available online, two of which are printable but are not available as electronic documents. Additionally, the paper summarising the review findings and listing all the consultation responses was too large to send electronically to your petitions e-mail account.

Therefore I have attached a link to these three documents below ahead of sending you hard copies.

These are for: -

- the frequently asked questions section of the cervical cancer screening page and
- the UK National Screening Committee membership and terms of reference
- the review summary and consultation responses

Please do get in touch regarding the appropriate postal address and if there is any additional information you require from the UK NSC.

Kind regards,

Hugh

NSC UK National Screening Committee

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Mr William Powell AC/AM
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13 August 2015

Dear Mr Powell

Thank you for your enquiry regarding the 2012 UK NSC recommendation to increase the age of first invitation for cervical cancer screening.

I have provided some information below, and attached documents detailing the consultation process underpinning this recommendation.

The three month public consultation was opened to stakeholders and the general public on the 10th May and closed on the 10th August 2012. It is worth noting that many of the 30 consultation responses we received were from NHS or professional organisations in Wales, who were supportive of the recommendation to start cervical screening at 25. These included: the Welsh Medical Committee, the British Medical Association of Wales, the Royal College of General Practitioners Wales, Public Health Wales, Powys Teaching Health Board, the Welsh Pharmaceutical Committee, the Welsh Nursing and Midwifery Committee, Cardiff and Vale University Health Board and Velindre Trust.

Following the consultation, the review papers and subsequent consultation responses were discussed by the UK National Screening Committee on the 13th November 2012, who approved the recommendation to extend the first invitation for screening from 20 to 25 years old in Wales and Scotland.

It was noted upon reviewing the consultation responses that, while the professional organisations were clear about the reasons to raise the initial age of screening, there was a lack of understanding as to the purpose of cervical screening in some of the public responses received. So during the consultation period further clarification was provided using these FAQs to explain the aim of screening and the rationale for the change in screening.

These include: -

- The review finding evidence that screening women under the age of 25 causes more harm than good.

- That the correct management or treatment for suspected cancer is not a screening test.

- What would make the biggest difference to survival for young women with cervical cancer is for symptoms to be recognised and treated. *(To this end all GPs in Wales have been reminded of the appropriate action in suspected cervical cancer or abnormal bleeding).* There is guidance for GPs to follow in identifying and sending selected cases directly to specialist care.

- Screening is not a test for cancer, but for abnormal cells which if left untreated can develop into cancer. However, these cells are very common in younger women and in the vast majority of cases will clear up of their own accord.

- If the results of a cervical screening test show abnormalities, the follow-up investigations may increase the risk of women subsequently suffering premature labour.

- It is now known that almost all cervical cancer is caused by HPV and since 2008 a vaccination programme has been underway for teenagers, which will greatly reduce their risk of cervical cancer when they are older.

Please see attached documentation including: the UK NSC minutes of the meeting where revised age for the first invitation to cervical screening was discussed, a paper summarising and listing all of the responses received as part of the consultation and the review papers that were originally considered by the UK NSC at this meeting. The latter papers include the discussion paper provided by the Welsh cervical screening programmes, the UK NSC review paper summarising the evidence and a PowerPoint Presentation using evidence to compare the impact that a programme with a first invitation to screen at 20 would have in comparison with one starting at 25.

I hope this information is of help and please do not hesitate to get in contact again should you require further information regarding this enquiry.

Yours sincerely

David Walker
Chair, UK National Screening Committee

Discussion Paper on Age of First Invitation for Cervical Screening and Frequency of Invitation of Cervical Screening for Women aged 50 to 64 years

Authors: Dr Sharon Hillier, Miss Helen Beer, Dr Shantini Paranjothy, Dr Rosemary Fox, Mr Bryan Rose and Professor Hilary Fielder. Screening Division Public Health Wales NHS Trust

Based on papers prepared by Professor Hilary Fielder and Mr Huw Brunt

Date: May 2011 | **Version:** 1

Publication/ Distribution:

- Public Health Wales (Intranet)
- Welsh Assembly Government

Review Date: Review in May 2012 or sooner if new information or evidence is available.

Purpose and Summary of Document:

The current policy for Wales is that women aged between 20 and 64 years are invited for cervical screening every three years. Scotland invite women aged between 20-60 years every three years. England and Northern Ireland invite women from 25 years of age and reduce the frequency of invitations to every 5 years for those aged between 50 and 64 years.

The purpose of this document is to review the evidence on which the age of

invitation and frequency of invitation is based and to discuss the implications of changes for the female population of Wales, for Cervical Screening Wales and for NHS Wales.
Work Plan reference: Cervical Screening Wales, Screening Division.

1 Executive Summary

This paper reviews the evidence base for the current cervical screening policy in Wales to ensure that waste, harm and variation are minimised.

Two distinct changes to the cervical screening programme are discussed:

- increasing the age of first invitation to screening from age 20 years to age 25 years
- increasing the screening interval for women aged 50-64 years from three years to five years.

These issues are considered independently.

The overall evidence base on which these changes are discussed is not strong as it derives from observational studies. However it is not realistic to expect that there will ever be randomised controlled trial evidence on which to base the decisions. Therefore the decisions need to be based on the balance of benefits and harms of the policy for the population.

Cervical Screening Wales considers that based on the current evidence the decision to increase the screening interval for women aged 50-64 years from every three years to every five years is highly acceptable.

Cervical Screening Wales considers that based on the current evidence regarding screening women aged 20-25 years, the balance of harms for the population outweighs the balance of benefit. As the population that has been offered Human Papillomavirus (HPV) vaccination reaches age of invitation to cervical screening, this balance of harms to benefit is more pronounced. The catch up population offered HPV vaccination at age 17/18 years in 2008 have been entering the programme from 2010 and the routine HPV vaccination at age 12/13 years will be entering the programme from 2014.

2 Context

The current cervical screening policy for Wales is that women aged 20-64 years are invited for screening every three years. The policy in Scotland is to invite women aged 20-60 years every three years. In 2003, England changed to invite women aged 25-64 and to standardise the frequency of invitation for those aged 50-64 to every five years. The decision for increasing the first age of invitation was based on a case control study published in 2003 which concluded that screening was less effective for young women.[1] Also there were concerns that as many young women had cellular changes that resolved spontaneously, screening could lead to unnecessary treatments, which could be a factor in premature delivery of subsequent pregnancies.[2] The decision for decreasing the frequency of screening from age 50 was based on results from the case control study published in 2003 which also concluded that five yearly screening offered similar protection to 3 yearly in this older age group.[1] In July 2010 Northern Ireland announced that they would change to the same policy as England from January 2011.[3]

The decision to change the age of invitation has been controversial and there has been a lot of public and press interest. This was heightened following the publicity around the death of the celebrity Jade Goody, who died from cervical cancer in 2009, aged 27. Following campaigns to lower the screening age from Jo's Trust and others, the Department of Health in England asked its National Advisory Committee on Cervical Screening to review the evidence. This was to ensure that the policy on starting screening at age 25 remained in the best interests of young women and was based on the latest available clinical evidence. The review took place at an extraordinary meeting of the Department of Health National Advisory Committee on Cervical Screening in May 2009 and concluded that the starting age of screening should remain at age 25.[4]

Scotland has convened an 'Age and Frequency of Cervical Screening subgroup' and the group has not made a decision to change the current policy and therefore women aged 20-60 years in Scotland are invited every three years.

The purpose of this paper is to review the evidence on which the age of invitation and frequency of invitation is based and to discuss the implications of changes for the female population of Wales and for the Cervical Screening Wales programme.

3 Background

3.1 Screening

Screening is a process of identifying apparently healthy people who may be at increased risk of a disease or condition. They can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition.[5]

The UK National Screening Committee (UK NSC) advises Ministers and the NHS in the four UK countries about all aspects of screening. Using research evidence, pilot programmes and economic evaluation, it assesses the evidence for programmes against a set of internationally recognised criteria covering the condition, the test, the treatment options and the effectiveness and acceptability of the screening programme. Assessing programmes in this way is intended to ensure that they do more good than harm at a reasonable cost. The UK NSC also regularly reviews policy on screening for different conditions in the light of new research evidence becoming available. [6]

The Welsh Assembly Government takes advice from the UK NSC and makes the decision whether the screening programme is implemented for the population of Wales. The UK NSC recommends cervical screening to be undertaken but does not comment on the appropriate age range of frequency of invitation.

3.2 Cervical Cancer

3.2.1 Natural History

Cervical cancer is caused by Human Papillomavirus (HPV) which is a sexually transmitted infection. Persistent infection by high-risk HPV types is detectable in more than 99% of cervical cancers.[7]

The majority of high-risk HPV infections are transient and cause no clinical problems. Within one year, around 70% of new infections will clear and approximately 90% of new infections will clear within two years.[8,9] However, persistent infection by a high-risk HPV type is the most important causal factor for the development of cervical pre-cancerous and cancerous lesions.

Cervical intraepithelial neoplasia 1 (CIN 1) is a histologic diagnosis associated with benign viral replication and in most cases spontaneously regresses. Studies in adult women show regression rates of 70-80%

whereas in adolescents and young women show more than 90% regression.[10]

Cervical intraepithelial neoplasia 2 (CIN 2) is regarded as a precancerous lesion although many of these are known to regress. The annual regression rate of CIN 2 in adult women is estimated to range from 15%-23% with up to 55% regressing by 4-6 years.[10]

Cervical intraepithelial neoplasia 3 (CIN 3) is considered a true precancer with the potential to progress to invasive cancer at the rate of 0.2% to 4% within 12 months. (10) Progression times from CIN 3 to invasive carcinoma vary between 5 to 19 years. [11,12,13]

3.2.2 Risk Factors

The risk factors for cervical cancer are having sexual intercourse at a young age, having many sexual partners, not using condoms and smoking.

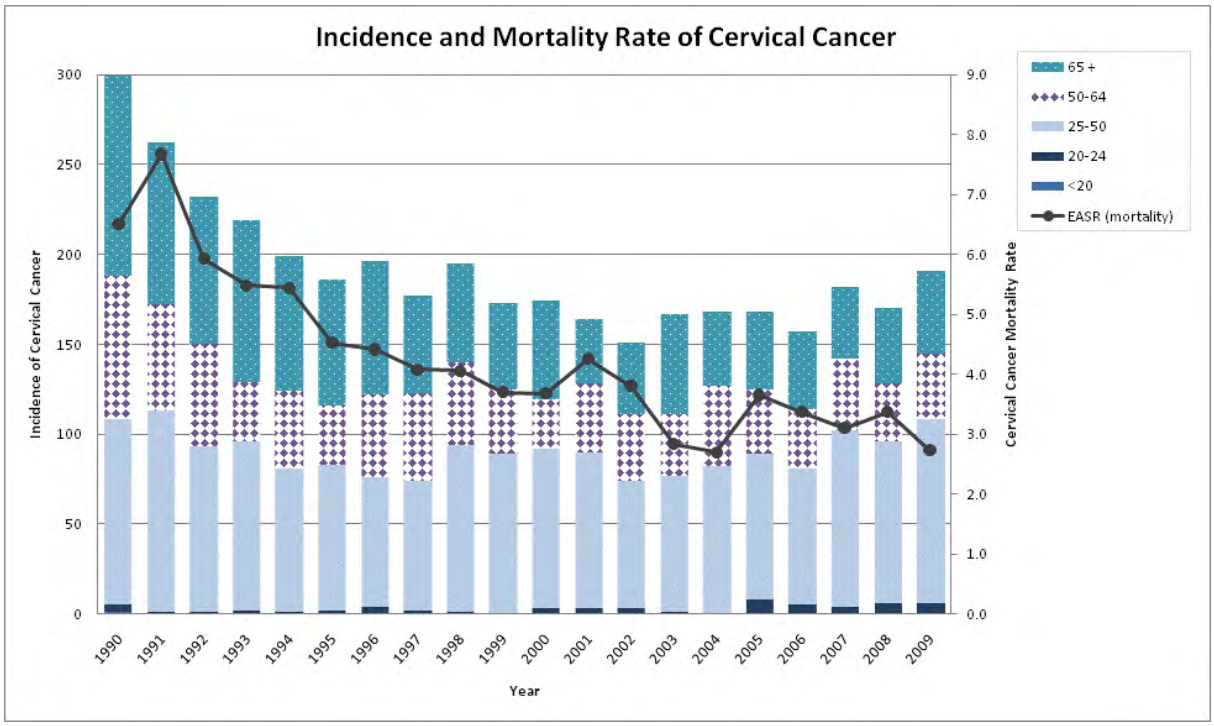
The 2006 Health Behaviour in School-aged Children Study showed that Wales had the fourth highest proportion of 15 year olds reporting having had sexual intercourse, (41% of girls and 30% of boys) out of 34 European and North American countries, and was higher than both Scotland and England.[14]

Young people (aged 16-24 years old) are the age group most at risk of being diagnosed with a sexually transmitted infection, accounting for 65% of all chlamydia, 50% of genital warts and 50% of gonorrhoea infections diagnosed in genitourinary medicine clinics across the UK in 2007.[15]

In 2008 it was estimated that 24% of people in Wales were smokers. Smoking is generally more common in younger people with more than twice as many 16 to 24-year olds being smokers (24%) compared to people aged 65 and over (10%).[16] Also, 12% of girls aged 13 in Wales reported that they smoked every week, which is twice the international average of 6%.

3.2.3 Epidemiology of Cervical Cancer in Wales

Figure 1



Sourced from WCISU data

Figure 1 shows the incidence of cervical cancer by age group from 1990 to 2009 and the European age standardised mortality rate. As can be seen the European age standardised mortality rate for cervical cancer has approximately halved since 1990.

With respect to the age of diagnosis of cervical cancer, the overall trend is that there were approximately half the number of diagnosis in the 65 year and older group and 50 to 64 years age group when comparing 1990 to 2009. However the 25 to 50 year old group does not show a sustained decrease and has similar incidence in 1990 compared to 2009. Although there are few diagnosis of cervical cancer for women aged between 20 and 24 years, over the time period shown, there has been a sustained increase in the incidence in this age group from 2005 to 2009.

The mean age specific rate per 100,000 for women aged 20-24 years for the time period 2005 – 2009 was 5.9.

3.2.4 Epidemiology of CIN2 and CIN3

The incidence of CIN3 has been increasing since the late 1980s in young women aged less than 35 years.[17] Prevalence of CIN 3 has increased in women aged 20-24 years which is consistent with more women in recent birth cohorts starting sexual activity in their mid teens. In England, there were over 3,000 women in 2002 that were registered with CIN3 in age group 20-24 years.[18]

The cohort of women resident in Wales aged 25 years at 1st Feb 2011, who had been ever been referred and treated in colposcopy (this was not limited to specific dates), either via screening or symptomatic services were reviewed to investigate the prevalence of CIN2 and CIN3 in this cohort. There were 20,225 women resident aged 25 years at 1st Feb 2011 and 1,725 had been referred to colposcopy previously, 1528 were referred as a result of an abnormal smear. Of those referred 302 (1.5%) had CIN2 diagnosed and 538 (2.7%) had CIN3 diagnosed. There were 16 diagnoses of cervical glandular intraepithelial neoplasia (CGIN) and 8 diagnoses of cervical cancer.

4 Cervical Screening Wales

4.1 Aim of Cervical Screening Wales

The aim of Cervical Screening Wales is to reduce the incidence of, and morbidity and mortality from, invasive cervical cancer.

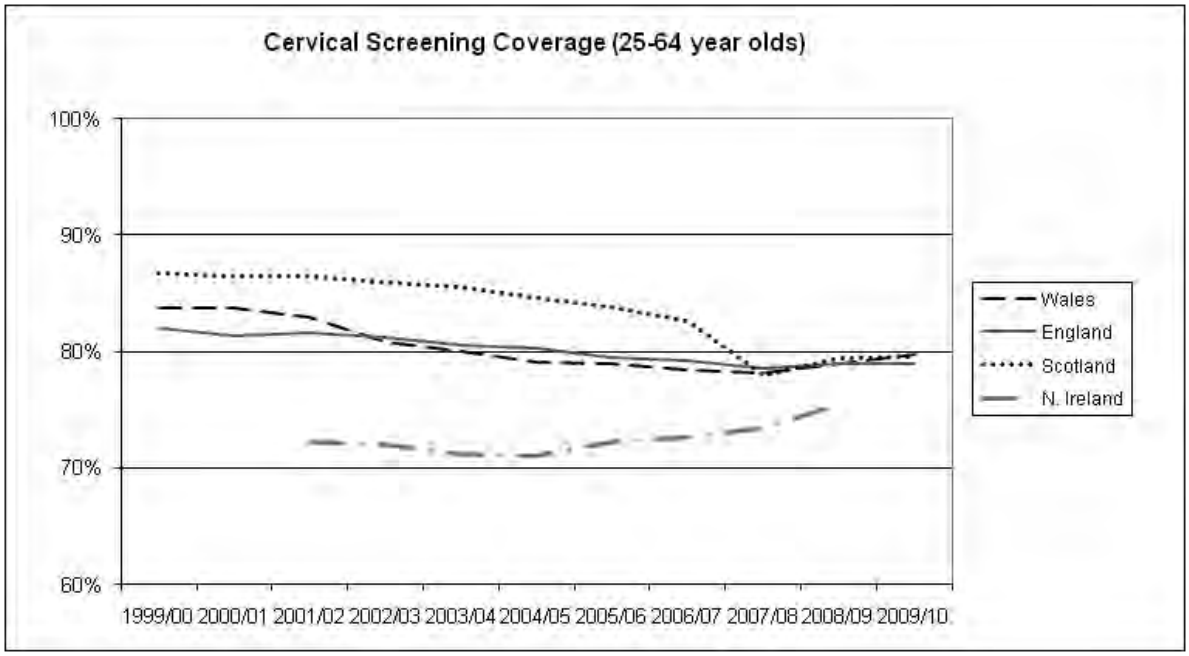
That is to undertake secondary prevention for cervical cancer by identifying cervical intraepithelial neoplasia lesions and treating these to prevent cancer from developing. On colposcopy some cancers are detected and although it is beneficial to treat these early (tertiary prevention) this is not the main reason for the cervical screening programme. Secondary and Tertiary prevention will be discussed separately.

4.2 Method

Women aged 20 to 64 years are sent an invitation letter to attend for a cervical screen every 3 years. Women can attend their General Practice or their local NHS Community & Sexual Health Clinic for a smear to be taken by a smear taker. The aim of the test is to detect early cell changes that may lead to cancer. The results are sent back to the women by post and if indicated the woman may be asked to attend for a repeat smear, or referred by Cervical Screening Wales to a colposcopy clinic for further investigation.

4.3 Coverage

Figure 2: 5 year Coverage for 25-64 years olds across UK for cervical screening (Data provided by screening information team, Screening Division)



The target standard in Wales is that 80% of eligible women aged 20 to 64 years have been adequately screened in the previous 5 years. Coverage is the proportion of people resident and eligible at a particular point in time who have been screened at least once in a defined time period.

The coverage rate of cervical screening in different countries of the UK is shown in Figure 2. This shows that for England, Wales and Scotland there has been a decline in the coverage rate over the last ten years. From 2000 to 2007 Scotland (invites up to age 60 years) has had the highest coverage of all of the countries and was consistently above the 80% target. England was above the target at the beginning of the period but dropped below 80% in around 2004/05 and then stabilised at about 79%. Wales was above the target until 2003/04 then dropped below 80% and remained below 80% until in 2007/08 when the coverage increased and nearly reached the 80% target in 2009/10. From 2001/02 to 2005/06 Northern Ireland had a stable coverage from 72% to 71% and was consistently lower than the other countries.

5 Age of First Invitation for Cervical Screening

5.1 Current Policies in the UK

The current policies in the UK for age of first invitation for cervical screening is 25 years of age for England and Northern Ireland and 20 years of age for Scotland and Wales.

5.2 Guidance

The UK National Screening Committee has not specifically advised on age at first invitation to cervical screening.

The Advisory Committee on Cancer Prevention of the European Union concludes that screening should be concentrated in women aged 30-60 years and definitely not to include women younger than 20 years.[19]

The American Cancer society published guidelines in 2002 and recommended that cervical screening should either begin at the age of 21 years or 3 years after the initiation of sexual intercourse.[20]

The World Health Organisation review stated 'There is minimal benefit and substantial harm in screening below the age of 25. Organized programmes should not include women aged less than 25 years in their target populations.' [21]

5.3 Literature review

Library and knowledge management service, Public Health Wales NHS Trust undertook a literature review in January 2011, to identify relevant articles that discussed the benefits and harms of screening 20-24 year old women (appendix 1). 80 articles were identified and on reviewing the abstracts 35 articles were selected in full. In February 2010 the NHS Cervical Screening Programme published a critical review of the literature on the impact of cervical screening on young women.[22] This was a focused review and stated that it was not a systematic literature review. The identified literature will be discussed under the defined questions which are relevant to the issues of inviting women aged 20-24 years for screening.

5.3.1 Does inviting women aged 20-24 years reduce the incidence of cervical cancer?

The intended benefit of inviting women at age 20 years is that their incidence of cervical cancer is reduced in the future by detecting and treating early cellular changes. However, it is difficult to estimate how many cervical cancer cases are prevented as not all precancerous changes will progress. In a study investigating the rate of progression of CIN2, 95 women with a mean age of 20.4 years; 2% (95%CI 1-9%) of patients showed progression to CIN3 by year 1; 12% (95% CI 8-22%) showed progression by year 2 and 15% (95% CI 9-26%) showed progression by year 3.[10]

Evidence from observational studies

The existing literature is limited because there are no randomised controlled trials able to be undertaken to investigate the effect of age on the effectiveness of cervical screening. The landmark meta analysis from the International Agency for Research on Cancer[23] provided no details regarding the age dependence of the results but stated that age did not affect either the sensitivity of cytological screening or the distribution of the sojourn time of the disease.

Case control studies have limitations as 'they depend on the underlying rate of cervical cancer in women who choose not to be screened, and this may be higher or lower than in the general population.[24]' Much of the observational evidence on the protective effect of cervical screening at all ages is derived from case control studies.

The case control study published in 2003 by Sasieni et al [1] informed the decision made in England to invite women from age 25 years. A more recent analysis by the same authors [25] of 4,012 women aged 20-69 years with invasive cancer diagnosed in participating centres and two controls per case individually matched on age and area of residence. They found that there was no evidence that screening women aged 22-24 reduced the incidence of cervical cancer at ages 25-29 OR 1.11 (95% CI 0.83-1.50).

Sasieni's original study did not investigate the reduction in incidence of microinvasive cancers which are of particular importance in younger women, as fertility sparing options for treatment may be feasible.[17] However the more recent study did classify microinvasive cervical cancers as cases.

In 2006, a review of the evidence of benefit and harm of undertaking cervical screening in Wales for women aged 20-24 years was published. [26] A literature review was undertaken and Welsh data for the number of cases of CIN3 were examined and rates of invasive cervical cancer for young women calculated. The results were that following the introduction

of the Welsh organised call/recall cervical screening programme, cervical cancer had reduced from 4.2 to 2.2 mean age-specific rate per 100,000 women aged 20 -24 years from 1981-88 to 1989-2003. The recommendations were to continue to invite women aged 20-24 years to cervical screening.

An Italian study in Florence [27] which compared the efficacy of screening women aged less than 40 and those aged 40 and older found that screening offered less protection to the younger women. A case control study in Australia found that screening every two years gave more protection for women aged over 30 years than those aged 20-29 years. However, the paper did conclude that there was benefit of screening women aged 20-29 years.[28]

A review of the Netherlands screening programme was published in 2008 [29] to determine whether the target age for cervical cancer screening should be lowered below the age of 30. All cervical cancer cases diagnosed in The Netherlands between Jan 1989 and Dec 2003 were selected and trends described. The authors concluded that because of the incidence and mortality rates for cervical cancer among women younger than 30 were low and not increasing, then the screening age for invitation should remain at 30 years of age.

A Swedish audit [30] found no evidence of screening being less effective in young women and found a 60% reduction in cervical cancer incidence.

A recent paper reviewed the Icelandic experience [31] with respect to age-specific effectiveness, optimal targeted age range and intervals in cervical cancer screening using data from the screening programme with centralised records dating from 1964. The findings confirmed a significant increased rate in the screened population of CIN 2, CIN 3 and microinvasive cancer since 1979, mainly in the age group 20-34 years and that the lesions started to accumulate within 3 years of a normal smear. The study concluded that the lower age limit of 20 years should remain unchanged.

Evidence from modelling studies

Canfell *et al* [32] predicted the impact of the 2003 changes in cervical screening practice in England on cervical cancer incidence rates using a markov stimulation model. Overall the predicted cumulative lifetime incidence of invasive cervical cancer in the UK was 1.7% in the absence of screening and 0.77% with the pre-2003 screening practice. A reduction in lifetime incidence to 0.63% was predicted following the implementation of the 2003 NHSCP recommendations. However, the benefit modelled was due to standardisation of the 3 year screening interval for women aged 25-49 years across England, which is standard practice in Wales anyway.

The model showed that screening women aged 20-25 years once in the 5-year period would have minimal impact with the cumulative lifetime incidence decreasing from 0.63% to 0.61%, even if coverage rates of over 75% were achieved in this age group.

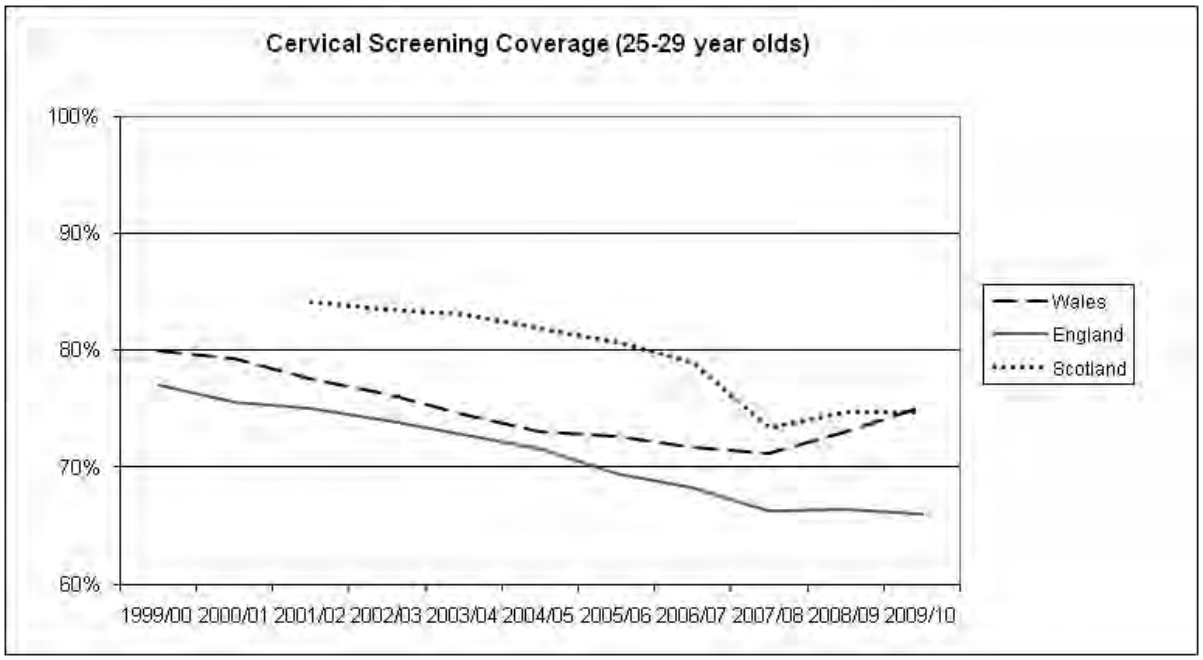
Peto *et al* [24] calculated the incidence and mortality for cervical cancer that would have occurred in England and Wales without the organised call and recall system implemented in 1988. Based on a cohort of women born in 1952, it was estimated that 1.5% of women would have died of cervical cancer before the age of 85, if they had never been screened, and 3% would have developed the disease.

Sasieni et al 2008 [33] estimated the cervical cancer rates that would have occurred in the absence of screening women aged 20-24 years using assumptions and past data on CIN registrations in England and Scotland from 1989 to 2004. The estimate was that at most 1.5% of women treated (equivalent to 3% of CIN3 registrations) would have had cancer by age 25. This data did not include welsh residents and did not model the numbers of cancers that would have been prevented in older age groups.

Estimation from Wales programme in 2006 [26] were that the Cervical Screening Wales potentially prevents one cancer and detects two micro-invasive cancers in the 20-24 year age group and prevents eight cancers in the 25-29 year age group each year. To achieve this 22,000 women in the age group 20-24 year old were tested each year and around 450 underwent large loop excision of the transformational zone (LLETZ). This estimate has been updated in section 4.4.3.

5.3.2 Does inviting women aged 20-24 year maintain and improve coverage in the future?

Figure 3 Cervical Screening Coverage for 25-29 years olds across UK countries. Data provided by screening information, Screening Division



Women aged 25-29 years have been shown to benefit from cervical screening [25] and it is important that the coverage rate for these women is sufficient. It is feasible that changing to inviting women from age 25 may affect the coverage of the cohort aged 25-29 years. Although it is not possible to evidence this effect, the trend of coverage across the UK shows variation between the different countries.

Figure 2 shows that overall Scotland has the higher coverage rate in the aged group 25-29 years although this has been reducing over time and in 2005/6 fell below the 80% target. England and Wales have been below the 80% target for the last 10 years and has been reducing over time with England having a consistently lower coverage than Wales. The difference between England and Wales was greater from 2005 and indeed from 2007 Wales has reversed the reduction with a marked improvement in coverage compared to England whose coverage has stabilised recently. In Wales there has been recently been a programme of work organised by the screening promotion team on increasing uptake in younger age groups and the downward trend has been reversed. Maintaining this coverage and working toward the target 80% is important to reduce the incidence of cervical cancer. It is possible that changing to inviting women to aged 25 years has reduced the coverage for this age group in England.

5.3.3 Does inviting women aged 20-24 years identify cervical cancers early (tertiary prevention)?

Although tertiary prevention of cervical cancer by identifying the cancers early is an advantage, this is not the main aim of the cervical screening programme.

A 12 year follow up study in the UK between 1985 and 1996 showed a reversal in the ratio of symptomatic to screen-detected cancers in women aged 25-34 years but no fall in the numbers of cancers.[34] This was interpreted as a clinical benefit as most screen detected cancers were diagnosed at an early stage with potential fertility conservation and good life expectancy prognosis.

In Guys and St Thomas' NHS Foundation Trust from 1999 to 2006 24 of 32 cancers in women aged 20-34 years were screen detected and that percentage declined in subsequent 15 year age bands ($p <= 0.0001$).[35]

In the paper by Sasieni [1] they looked in detail at 34 women with cervical cancer aged 20-24 years; 26 of these had a previously operationally negative smear. A review of the screening histories of the 13 women with stage 1B+ cervical cancer in this age group indicated that six of these cases were symptomatic.

5.3.4 Does inviting women aged 20-24 years affect birth outcomes for subsequent pregnancies?

For women in this age group there is concern about the possible impact on colposcopic interventions for future pregnancies. In a critical review of the literature published by the NHS Cervical Screening Programme[22] conflicting results from studies were reported. In 2007 a systematic review and meta analysis [36] of 27 studies found that LLETZ was significantly associated with preterm delivery with an overall Relative Risk of 1.70 (95% CI 1.24 -2.35). In the five further primary research studies conducted after the meta analysis four found that treatment was associated with an increased risk of preterm delivery and one found that the diagnosis of CIN3 was associated with preterm delivery and not treatment itself. [22] The majority of studies have been limited in their ability to take into account potential confounding factors that could be independently associated with being referred for colposcopy and preterm delivery for example maternal smoking, socioeconomic status and previous obstetric history.

A study to investigate this issue in Wales was undertaken by Screening Division and Cardiff University in collaboration with Swansea University [37] The aim was to investigate whether treatment for precancerous changes to the cervix were associated with preterm birth in subsequent pregnancies in 174,100 women aged 20-39 years in Wales who received cervical screening between April 2001 and March 2004. The study found that compared to women who had negative cervical smears, the odds ratio for preterm birth (less than 37 weeks) was significantly increased in women who had colposcopy only (adjusted OR 1.54, 95% CI 1.32-1.80) and single excisional treatment (adjusted OR 1.77, 95% CI 1.47-2.13). Among women who were referred to colposcopy for abnormal cervical smears there was no increased risks of preterm birth or low birth weight for women who had treatment compared to women who had colposcopy and punch biopsy only. The study's conclusion was that the increase risk of preterm births may be explained by other characteristics of women who had abnormal smears.

5.3.5 Does inviting women aged 20-24 year increase their anxiety?

It is reported in the literature that women who receive an abnormal smear result have increased anxiety, and their worries include fear that they have cancer, self blame, sexual guilt and concerns about infertility.[38] Most research has been on high grade abnormal smears however a study looking at 3500 women recruited to Tombola (trial of management of borderline and other low grade abnormal smear) found that women reported anxiety levels for low grade abnormal smear results which were consistent with those found in previous studies of women with high grade abnormal smear results. Stratification of the effect of age on anxiety was not discussed in any of the identified studies.

Also there were no studies identified that discussed the effect of different policies across the UK on age of invitation, as young women may have been anxious especially following media attention of the recent celebrity death from cervical cancer.

5.4 Description and outcome of Cervical Screening for 20-24 year olds in Wales

5.4.1 Secondary prevention of cervical screening

Coverage of Cervical Screening

As of 31st March 2010 there were 106,573 eligible women resident in Wales aged 20- 24.

The coverage rate of cervical screening in 20-24 year olds in Wales is lower than the overall rate for women aged 20-64 years. As of 31st March 2010, 54,123 (50.8%) of women aged 20 -24 years had a smear test within the last 3 years and 57,752 (54.2%) had a smear test within the last 5 years. Comparing this with the age group 25-29 years; 64,420 (65.3%) had a smear test within the last 3 years and 74,028 (75.1%) had a smear test with the last 5 years.

The overall rate for women aged 20-64 years for the same time period was 66.7% within the last 3 years and 76.5% within the last 5 years.

Results of the cervical screening

For the year April 09- March 2010, there were 31,139 adequate samples examined by the pathology laboratories from 20-24 year old women. Of these

25,472 (79.3%) were negative and would have routine recall in 3 years or annual smears

3,680 (11.5%) had borderline changes and repeat smear requested or referral

2,106 (6.6%) had mild dyskaryosis and repeat smear requested or referral

452 (1.4%) had moderate dyskaryosis and were referred to colposcopy

415 (1.3%) had severe dyskaryosis and were referred to colposcopy

14 (<0.1%) had query invasive carcinoma or glandular neoplasia and referred to colposcopy.

Therefore 21.7% of the women who had cervical screening had a further intervention following the results.

Outcomes of cohort of women, currently aged 25 years, referred to colposcopy

The cohort of women aged 25 years and residents in Wales on the 1st of February 2011, who had ever been referred to colposcopy as a result of an abnormal smear, were followed up to review their outcomes. Databases were interrogated to obtain outcomes for women who attended colposcopy in Wales and those who attended colposcopy in England. Where a woman had multiple referrals the information about the woman's treatment and diagnosis was restricted to the same episode. Where a woman had two different abnormal referral smears these were counted as two episodes.

There were 1,774 referrals for 1,636 women and the worse outcome was CIN1 368 (20.7%), CIN2 298 (16.8%), CIN3 522 (29.4%), CGIN 16 (0.9%) and 7 (0.4%) cancers were diagnosed. 949 (53.5%) referrals resulted in treatment and 733 (41.3%) of these were for a LLETZ procedure.

The predictive positive value (PPV) can be calculated from the data to correlate high-grade cytology with histology. It records the proportion of cases in which a biopsy, following a screening test reported as moderate dyskaryosis or worse yield a histological diagnosis of CIN2 or worse. The PPV for the cohort of women age 25 years was 80.7% which was lower than the average PPV for Wales which was 83.3% for the time period 2005-2010.

The PPV for a histological diagnosis of CIN3 or worse for the cohort of women aged 25 years following a screening test, reported as moderate dyskaryosis or worse was 58.6%.

Overall the PPV for a histological diagnosis of CIN3 or worse for this population following an abnormal smear result, which prompted a referral for colposcopy, was 30.7%. This is low because the PPV for diagnosis of CIN3 or worse was low for those women identified with low grade dyskaryosis or borderline changes at 12.4%.

5.4.2 Tertiary prevention of cervical screening

Two separate look back exercises were undertaken for cervical cancer registrations in Wales in women aged less than 29 years, registered in 2007 and 2009. Age less than 29 years was chosen as one of the expected benefits for screening women aged 20-24 years is to reduce the risk of them developing cancer when older.

Cervical cancer registration in 2007 and aged less than 29 years

In 2007 there were 182 cervical cancer registrations in Wales and 19 of these were less than 29 years of age (10.3%). At the time that the look back exercise was undertaken there were 17 on the cervical cancer register and it assumed that the remaining two were added at a later date.

An audit of these 17 registrations found that 12 of the 17 registrations were screen detected (70.6%) with 6 micro invasive cancers and 11 invasive cancers diagnosed. Only 4 of these were regular screeners and 8 were lapsed screeners. 3 of the 17 women were known to have died and none of these women were screen detected cancers, 2 of the women had never been screened and 1 was a lapsed screener.

Three of the registrations were women aged between 20 and 24 years. Two were regular screeners and the cancer was identified by screening and one was a lapsed screener whose cancer was not identified by screening. This young woman was known to have died.

Cervical cancer registration in 2009 and aged less than 29 years

In 2009 there were 191 cervical cancer registrations in Wales and 24 of these were less than 29 years of age (12.5%).

An audit of these 24 registrations found that 19 were known to be screen detected (79%) with 9 micro invasive cancers, 6 invasive cancers, 2 adenocarcinomas, 1 not stated and one squamous cell cancer. Only 4 of these had been screened at the correct age intervals, remaining were lapsed screeners. Two of the 24 women registered with cervical cancer were known to have died and both these women had never been screened.

Six of the registrations were women aged between 20 and 24 years. Four women had their cancer diagnosed by screening and all were lapsed screeners. The remaining two women were diagnosed following symptomatic referral with one of the women never attending screening. This young woman was known to have died.

In summary these two look back exercises show that 71% and 79% of the cancers found in this age group were screen detected. Although this is not the primary aim of the screening programme the benefit of tertiary prevention does need to be considered for this population.

5.4.3 Estimation of benefit and harm of Cervical Screening Wales

The outcome data shows that for the cohort of women who were aged 25 years as of 1st February 2011 and invited to screening from age 20 years, there were 1,774 referrals following an abnormal smear result and 949 referrals resulting in treatment. In this cohort there were 522 cases of CIN3 diagnosed. Using 0.2% as a minimum estimate and 4% as a maximum estimate of CIN 3 progressions to invasive cancer each year (10); the range of number of cancers prevented would be 1 to 21.

5.5 Implication of changes to age of invitation of screening for Cervical Screening Wales

The implications of changing the first age of invitation for cervical screening from age 20 to age 25 are discussed with reference to the workload predictions.

The model is based on changing the call age from age 20 to age 25 at a defined point in time. Women aged between 20 and 25, who have already been invited to cervical screening, will continue to be invited as it would be unethical to stop once they were in the programme. This would mean that 21 year olds due to be sent reminder letters or early repeat smears would still be invited and women due for recall at age 23-24 will be sent their 3 year recall invitation. From the defined point in time there would be no new 20 year olds entering the programme.

The estimations of workload have been modelled for 6 years from the point of change for number of invitations, number of smear tests and colposcopy referrals. The average numbers from 2005 to 2010 have been used as the estimate on which to base the model and this does not take into account fluctuations in the population over time.

The set up of the model is that in year one the cohort aged 21-24 are invited as currently policy but no new 20 year olds are invited; in year two the cohort now aged 22-24 are invited as current policy but no new 20 or 21 year olds are invited; year three the cohort aged 23-24 remain invited but no new 20,21 or 22 year olds are invited; year four the cohort aged 24 remain invited but no new 20,21,22 or 23 year olds; in year five the cohort aged 25 and those aged 24 and 11 months are invited to the programme but no new 20,21, 22, 23 or 24 year olds; in year six the cohort aged from 24 years and 11 months have their first invitation to the programme.

It is assumed that the uptake rate and abnormal cytology detection rate remains unchanged in the age groups. This may not be the case and if more women have abnormal cytology at age 25 because they have not

been screened at ages 20-24 years, then this will need to be taken into account. There will be a small number of women that move into Wales that are currently called by CSW under 25 years that would be excluded in future, these have not been taken into account in the model. The effect of screening a population who has been offered HPV vaccination and the effect of using HPV testing is not within the remit of this model.

5.5.1 Modelling results

Number of Screening Invitations

Table 1 Invite women from age 25 years from implementation of change

	Average from 2005 to 2010	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total annual invitations all age groups	321406	306579	302519	293793	283673	277095	281690
Decrease per annum:		14826	18887	27613	37733	44311	39716 - 41616

Total decrease in cervical screening invitations over 5 years is estimated as 143,369

Years two, three and four are set as the minimum reduction predicted and are likely to be between the minimum and maximum reduction of 44311. This will be dependent on the time taken for women to respond to their invitation and the numbers being re-invited or re-tested based on their test result and this is difficult to predict.

Year 6 has the minimum reduction predicted as 39716 and maximum reduction of 41616 to take into account the potential increase in numbers of the cohort aged 25 years in six years time.

Number of Cervical Screening Tests

Table 2 Invite women from age 25 years from implementation of change

	Average from 2005 to 2010	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total annual tests all age groups	238288	229123	224064	219863	212839	207082	217582
Decrease per annum:		9165	14224	18425	25449	31206	20706 to 22206

Total decrease in cervical screening tests taken over 5 years is estimated as 98470

Years two, three and four are set as the minimum reduction predicted and are likely to be between the minimum and maximum reduction of 31206. This will be dependent on the time taken for women to respond to their invitation and the numbers being re-invited or re-tested based on their test result and this is difficult to predict.

Year 6 has the minimum reduction predicted as 20706 and maximum reduction of 22206 to take into account the potential increase in numbers of the cohort aged 25 years in six years time.

The model has assumed that the uptake rate remains unchanged when the policy is changed but this may not be the case.

Number of Colposcopy Referrals

Table 3 Invite women from age 25 years from implementation of change

	Average from 2005 to 2010	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total annual colposcopies in all age groups	8858	8527	8094	7740	7308	6835	7570
Decrease per annum:		331	764	1118	1550	2024	1289-1394

Total decrease in colposcopy referrals over 5 years is estimated to be 5787.

In year six if we assume 7% of women in the 25-29 age group that are tested are referred to colposcopy (based on our current experience of this age group) we would expect between 630-735 extra colposcopies in this age group in year six. Year 6 has the minimum reduction predicted as 1289 and maximum reduction of 1394 to take into account the potential increase in numbers of the cohort aged 25 years in six years time.

Modelling the colposcopy referrals this has included both women referred with abnormal cytology and those referred symptomatically. It is not known whether stopping screening at age 20 years will cause an increase in the number of symptomatic referrals to colposcopy in this age group. It is assumed that the uptake rate and abnormal cytology detection rate remains unchanged in the age groups. This may not be the case and if more women have abnormal cytology at age 25 because they have not been screened at ages 20-24 years, then this will need to be taken into account.

5.6 Future issues

5.6.1 HPV vaccination status

In October 2007 Welsh Assembly Government announced that all 12 to 13 year old girls would be offered vaccination against two HPV virus types that cause 70% of cervical cancer.[39] The following year a catch up programme for 17-18 years olds was initiated and this was further accelerated in March 2009. As at November 2010, uptake across Wales of the HPV vaccine in girls in the 2009-10 School Year 8 was 85%, 83% and 77% for one, two and three doses respectively.[40]

In 2014 the cohort of girls who were offered vaccination aged 12 to 13 will be approaching 20 and therefore will be invited for cervical screening under the current policy in Wales. It is expected that this population will be at reduced risk of cervical cancer and therefore the benefits and harms of the screening programme will be different and it is probable that the benefits will be reduced. However, vaccination does not protect against all HPV virus types that cause cervical cancer and the uptake of the vaccine will not be 100%; therefore this population will still be at risk of cervical cancer. The evidence that will be required to inform this decision will be uptake of vaccination, efficacy of vaccination and surveillance to ensure that other high risk HPV virus types are not causing disease.

5.6.2 HPV Testing

In 2011 the NHS Cervical Screening Programme in England will begin incorporating HPV triage into their screening programme.[41] The sentinel site implementation project tested samples from women which contained cells with low-grade abnormalities (borderline or mild dyskaryosis). If they tested positive for high-risk HPV strains they were referred for colposcopy and if they were negative for high risk HPV strains they could be returned to routine recall. Wales has not been one of the pilot sites and is not currently undertaking HPV testing.[41]

Other proposed uses for HPV test are 'test of cure' which will test for HPV following treatment and if negative the woman can have routine recall rather than yearly cytology follow up.

The main application for the HPV test that would have an impact on age of invitation would be using HPV as the primary test rather than cytology. As the prevalence of HPV infection is likely to be higher in younger women, using HPV as the primary test may not be sufficiency specific for this population. The studies published on using the HPV test as the primary test have studied population aged 25 years and older. It would not be

feasible to use HPV as the primary test for this population without robust evidence that it is an effective test in this aged population. There will also need to be work around the feasibility of triage and test of cure in the population aged between 20-24 years.

5.7 Summary

There is not a strong evidence base on which to make recommendations on the starting age for cervical screening. The observational studies indicate that screening is not as effective in women aged 20-24 years, as the identified cellular changes can spontaneously regress. However, it is not possible to predict which lesions will regress and there will be a minority of women who will have an identified CIN3 or worse and will likely benefit from treatment. The prevalence of CIN3 for the cohort of women aged 25 years in Wales at Feb 2011 was found to be 2.7% (538 diagnosed out of 20,225 residents).

The other argument is that this population are child bearing age and there is evidence that undergoing LLETZ procedure increase the risk of preterm delivery of subsequent pregnancy. However, the studies were unable to adequately control for potential confounders to demonstrate the causality of this relationship. Indeed the study conducted in Wales [37] concluded that the increase risk of preterm births may be explained by other characteristics of women who had abnormal smears.

The predictive positive value for a histological diagnosis of CIN3 or worse for the cohort of women currently aged 25 years following any previous screening test reported as moderate dyskaryosis or worse was 58.8%. Overall the PPV for the population aged 25 years for predicting CIN2 or worse following a screening test reported as moderate dyskaryosis or worse was 80.7% which was lower than the overall PPV for the whole age range for the same time period at 83.3%.

Considering the issue of harms it is important to note that the PPV for a histological diagnosis of CIN3 or worse for the cohort of women aged 25 years following a screening test reported as low grade dyskaryosis or borderline changes was low at 12.4%.

Although tertiary prevention of identifying cancers early in this age group is not the aim of the screening programme, in two look back exercises 71% and 79% of the cancers found in this age group were screen detected. The incidence of cervical cancer in the age group 20-24 years has increased since 2005 and the mean age specific rate was 5.9 per 100,000 from 2005 to 2009.

Recently Wales has reversed the downward trend of young women attending for their smears and there needs to be careful management of

information on which age women should attend screening to minimise confusion.

The balance of benefit versus harm will be further changed from 2014 as the cohort of girls who were offered vaccination aged 12 to 13 will be approaching 20 and therefore will be invited for cervical screening under the current policy in Wales. It is expected that this population will be at reduced risk of cervical cancer and therefore the benefits and harms of the screening programme will be different and it is probable that the benefits will be reduced. However, vaccination does not protect against all HPV virus types that cause cervical cancer and the uptake of the vaccine will not be 100%; therefore this population will still be at risk of cervical cancer.

If HPV testing is used as a primary test or as triage in Wales, the population aged 20-24 will have to be considered independently as currently there is a dearth of information of the appropriateness of these tests in this age group.

Making the change to inviting women from age 25 years will affect the workload for cervical screening, smear takers, cytology and colposcopy services and this will need to be actively managed to ensure that services remain sustainable.

6 Frequency of Invitation of Cervical Screening for Women aged 50 years and older

6.1 Current Policies in the UK

The current policy for Wales for women aged 50-64 years is that they are invited for cervical screening every three years. The policy in Scotland is to invite women aged 50-60 years every three years. In 2003, England standardised their policy to invite women aged between 50-64 years every five years. In July 2010 Northern Ireland announced that they would change to the same policy as England from January 2011 (3).

The screening interval is different in different countries with USA having annual screening, Australia 2 yearly and Finland five yearly.

6.2 Guidance

The UK National Screening Committee has not specifically advised on frequency of screening for women aged over 50 years.

6.3 Description and outcome of Cervical Screening for women aged 50 years and older

The coverage rate of cervical screening in 50-64 year old in Wales:

Of the 243,448 eligible women resident in Wales at 31st March 2010 aged 50-64 years; 166,389 (68.3%) had a smear test within the last 3 years and 191,020 (78.5%) had a smear test within the last 5 years.

Of the 56,295 adequate samples from 50-64 year old eligible women, examined by the pathology laboratories from April 09- March 10, 54,399 (96.6%) were negative; 1,297 (2.3%) had borderline changes; 383 (0.7%) had mild dyskaryosis, 93 (0.2%) had moderate dyskaryosis; 78 (0.1%) had severe dyskaryosis; 11 (<0.01%) had query invasive carcinoma and 34 (0.1%) had query glandular neoplasia.

6.4 Effect of frequency of screening for women aged 50 years on benefits and harms of Cervical Screening

6.4.1 Literature review

In January 2011 the Library and Knowledge Management Service Public Health Wales, NHS Trust undertook a literature search to identify studies that describe the benefit and harms of changing cervical screening frequency from 3 to 5 years in women aged 50 year or older. The search identified 59 articles (Appendix 2), the abstracts of these were reviewed and 17 articles requested in full. The 17 articles were reviewed and other relevant articles identified and requested. The articles informed the discussion as detailed.

6.4.2 Will increasing the screening interval effect the incidence of cancer?

The evidence on which the screening interval was based was originally an international study conducted by the IARC that estimated yearly screening reduced the incidence of invasive cervical cancer by 94%, three yearly by 91%; five yearly by 84% and 10 yearly by 64%.[42]

In 2003 two studies were published which provided more evidence on screening frequency. The first paper (2) analysed screening histories of 1305 women aged 20-69 years, diagnosed with frankly invasive cervical cancer and 2532 age matched controls obtained from the UK screening programme database. Their analysis showed that by using time since the last operationally negative cytological smear 4.5 to 5.5 yearly screening offered 72% (95% CI 43%-86%) protection compared to 2.5-3.5 yearly screening protection of 85% (95% CI 74%-92%) for women aged 55-69 for frankly invasive cervical cancer.

The authors produced summary point estimates of protection and concluded that five yearly screening offered similar protection to 3 yearly. It is on the results of this paper that England standardised to inviting women aged 50-64 year every 5 yearly. This paper has age groups in 55-69 and the policy is 50 -64 to allow time from screening to cancer diagnosis. The issues are that the paper assumed that screening to cancer diagnosis does not vary by age from 50 to 55 years, the analysis did not include screen detected micro invasive cancers; there were 490 (18%) results that had cancer stage unknown which may have biased the results, and the data was from England and the population in Wales may be different.

A Dutch study published in 2004 [43] supported a five year screening internal by reporting that the incidence of squamous cell carcinoma and precursor lesions remained stable when changing from a 3 year to 5 year screening interval. However this study did not stratify the results by age.

A paper published in 2004 which modelled the effect of implementation of the 5 year screening interval at age 50 years supported the recommendation of changes to cervical screening intervals. [32] However the actual outcomes have not yet been reported.

Unpublished work undertaken with Sasieni *et al* and Cervical Screening Wales explored the effectiveness of the screening programme in Wales between 1999 and 2007. The odd ratios for screening between 1990-2001 were compared to those between 1999-2007 and population attributable risks were calculated. A total of 1,466 cases of cervical cancer were diagnosed in Wales between 1999 and 2007, 73% of which were diagnosed in women aged 20-64 years. There was no evidence to suggest that extending the screening interval from 3 yearly to 5 yearly in women aged over 50 years increased the risk of developing cervical cancer (0R 0.17, 95% CI 0.11- 0.27 vs, OR 0.14 95% CI 0.08-0.24 respectively).

6.4.3 Will increasing the screening interval affect coverage?

There was no information in the literature as to the effect of reducing the frequency of invitation to coverage of screening.

6.4.4 Will increasing the screening interval have an effect on anxiety of the women?

There was no information in the literature as to the effect of reducing the frequency of invitation to anxiety

6.5 Implications of changes of frequency of screening for women aged 50 years and older to workload of Cervical Screening Wales

The implications of changing the frequency of intervention for women aged 50 years and older for the workload of Cervical Screening Wales are outlined. three different models are outlined:

- **Model 1:** no change – keep three-year routine recall;
- **Model 2**: change to five-year routine recall from date next smear test result is entered;

- **Model 3**: change current routine recall invitation dates from three to five-yearly recall (i.e. add two years to date of next invitation);

Data were obtained from the Exeter call-recall system and via laboratory pathology reports. Average numbers of smears taken and analysed as a result of 'routine', 'early repeat' and 'other' recall types were calculated. Averages were based on data collected during a complete round of screening from 2004 to 2006.

The modelling assumed that numbers of 'early repeat' and 'other' recall test types were relative to the number of 'routine' recall tests taken in the previous year, the screening population remained stable over time; only the routine recalls in women afed 50 years and over changes in each model,the rate of opportunistic cervical screening remained unchanged over time; that women are exactly 50 years old or more on the day that the smear is taken; and that the uptake by women for five-yearly screening was the same as for three-yearly screening.

This modelling only looks at the effect on the number of smears taken and does not take into account the effect on cytology results and colposcopy referrals. The modelling includes the total population invited for screening.

6.5.1 Modelling results

Table 4 Total number of screening tests undertaken implementing change in Year 2.

MODEL	Year 1	Year2	Year3	Year 4	Year 5	Year 6	Year 7	Year 8	Year9	Year 10	Year 11	Year 12	Year 13	Year 14	Year 15	Year 16
1	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746	221746
2	221746	221746	221746	221746	179637	172061	211760	217122	218618	184550	176545	209013	214000	215960	188405	180382
3	221746	179637	172061	211760	217122	218618	184550	176545	209013	214000	215960	188405	180382	206896	211451	213655

Table 5 Differences in number of screening tests comparing model to baseline (model 1 no policy change)

MODEL	Year 1	Year2	Year3	Year 4	Year 5	Year 6	Year 7	Year 8	Year9	Year 10	Year 11	Year 12	Year 13	Year 14	Year 15	Year 16
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	-42109	-49684	-9986	-4623	-3128	-37196	-45201	-12732	-7746	-5786	-33341	-41363
3	0	-42109	-49684	-9986	-4623	-3128	-37196	-45201	-12732	-7746	-5786	-33341	-41363	-14850	-10295	-8090

The main issue with increasing the frequency of the interval is that the stable number of test undertaken each year would change to have a sequence of peaks and troughs. To explain the reason for this using model 3, in year 2 the cohort of women aged 50-64 years would have their tests delayed two years (creating a trough in numbers) and be invited in year 5 in addition to those routinely invited in year 5 (creating a peak in numbers). Each year the cohort of women reaching age 50 will also have their invitation delayed and this further impacts on the peaks and troughs as modelled.

The greatest reduction in workload would be expected from the implementation of the policy change using model 3. Model 2 predicts that there is likely to be no change to the number of tests undertaken in the first three years following a change to the existing policy.

It would be important for any policy change that burden on the administrative service areas of the screening programme needs to be avoided and efforts to ensure that there are clear messages to screen takers and other programme professionals to minimise confusion.

6.6 Future issues

6.6.1 HPV Testing

In 2011 the NHS Cervical Screening Programme in England will begin incorporating HPV triage into their screening programme.[41] The sentinel site implementation project tested samples from women which contained cells with low-grade abnormalities (borderline or mild dyskaryosis). If they tested positive for high-risk HPV strains they were referred for colposcopy and if they were negative for high risk HPV strains they could be returned to routine recall. Wales has not been one of the pilot sites and is not currently undertaking HPV testing.[41]

Other proposed uses for HPV test are 'test of cure' which will test for HPV following treatment and if negative the woman can have routine recall rather than yearly follow up.

The implementation of HPV as a primary test in the population aged 50-64 years needs to be modelled and it is possible that changing the testing method may improve the efficiency of cervical screening in this age group.

6.7 Summary

There is not a strong evidence base from randomised controlled trials on which to base the decision on screening interval for women aged between 50 and 64 years. The observational studies undertaken indicate that increasing the interval between screening invitations for this age group does not increase their risk of developing cervical cancer.

There was variation of screening intervals in England before 2003 and one of the benefits of introducing this policy was standardisation across England, there is standardisation already in Wales.

The uptake of women in this age group of cervical screening is good as 5 year coverage was 78% of eligible women resident in Wales at 31st March 2010. The prevalence of a test result indicating moderate or severe dyskaryosis was low in this age group at 0.2% and 0.1% respectively.

The argument made against screening women aged 20-24 years does not hold true for this population as they are not child bearing age and spontaneous regression of cellular changes are not an issue. Therefore, the issue is the efficiency of 3 yearly screening compared to 5 yearly screening.

7 Discussion

Two distinct changes to the cervical screening programme are discussed in this paper and the interconnection between these changes needs to be taken into account. Both changes if implemented will result in a decrease in invitations to screening, number of screening tests and resultant colposcopy referrals. These will need to be modelled in tandem to understand effects to the service if there are changes proposed.

The evidence base on which these changes are discussed are not strong as they are observational studies. However it is not realistic to expect that there will be randomised controlled trial evidence on which to base the decision. The overall benefits and harms for cervical screening needs to be considered for these two distinct populations.

This paper has not discussed the benefits and harms of screening women aged between 20 and 24 years who have been vaccinated against HPV and has not taken into account any other screening test methodology such as HPV as a primary test. The balance of harms and benefits will be different for a vaccinated population and these will need to be outlined. However, this will depend on how good the uptake of the complete vaccination course has been in this population. There will be issues around using HPV test on this population as there is currently no published data

on testing younger women in this way. Although the HPV vaccination will not be a factor in the decision to decrease the frequency of cervical screening for women aged between 50 and 64 years, the implications of HPV testing both as primary test, triage and test of cure will need to be explored.

8 Recommendations

1. Cervical Screening Wales (CSW), Screening Division makes the following recommendations to the Welsh Screening Committee for consideration:Screening policy in Wales should be altered to increase the screening interval for women aged women aged 50-64 years from every three years to every five years. This change should take place as soon as possible.

2. Screening policy in Wales should be altered to increase the age at first invitation from 20 to 25 years. Women who are aged less than 25 years and have already been invited to the screening programme should continue to be screened according to the current policy.

Implementation and timing of these changes should be managed in such a way as to

- ensure that the reduction in numbers can be managed by the service effectively
- ensure clear communication and training to professional groups who undertake the cervical screening
- ensure clear communication to the public especially to women who would be expecting to be called for screening and those who have been offered HPV vaccination

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Appendix 1

Topic: Cervical screening
Search question: ***1 To identify studies that describe the benefits and harms of cervical screening in women aged 20 -25 years. Including; cervical cancer incidence, cervical cancer mortality or morbidity, anxiety, cost effectiveness, birth outcomes for future pregnancies and coverage.***
For : Dr Sharon Hillier, Screening Division
By: Sian King, LKMS Swansea
Date : 26/01/11
Updated:

1.Methodology	
Search terms :-Keywords, Free text	Cervical screening Age adj4 25 Young adj women
Database subject headings:- MESH, HMIC	Ablation techniques/ae Cancer screening Carcinoma squamous cell/di, pc Cervical cancer Cervical cancer-prevention and screening Cervical intraepithelial neoplasia Cervical screening Cervix neoplasms, Cervix uteri/ab Cervical cytology

	Colposcopy Electrosurgery/ae Mass screening Papillomavirus infections Screening Screening programmes Screening services Squamous cell carcinoma Uterine cervical neoplasms Uterine cervix Uterine cervix cancer Uterine cervix carcinoma Uterine cervix carcinoma in situ Uterine cervix tumor Uterus cancer Vagina smear Vaginal smears Adolescent Age distribution Age factors Age of onset Early diagnosis Early detection of cancer Women Young people Young adults Anxiety

	Distress Costs Cost effectiveness High risk pregnancy Pregnancy complications Pregnancy high risk Pregnancy outcome Premature birth Risk factors Data Incidence of disease Incidence Statistical data Tabular data
Limits	
• Publication types	Guidelines, reviews, reports, articles
▪ Language	English
▪ Dates covered	2000-2011
▪ Geographical location	Worldwide (developed countries)
Other criteria	
Filters	

2. Sources	
(i) Core databases/sources	
BNI	27/01/11
CINAHL	27/01/11
Clinical Evidence	n/a
Cochrane Library	27/01/11
EMBASE	27/01/11
HMIC	26/01/11
MEDLINE	26/01/11
NICE	27/01/11
Library catalogue & knowledge base	26/01/11
PsycINFO	27/01/11
Public Health Wales Document database	

(ii) Topic specific databases, sources	
Databases	
Websites	
ACOG	27/01/11
Department of Health	26/01/11
National Breast and Cervical Cancer Early Detection Program	27/01/11

NI Cancer Screening Programme	27/01/11
NHS Cervical Screening Programme	26/01/11
NHS Evidence – specialist collection	28/01/11
NHS National Services Division (Scotland)	27/01/11
RCOG	27/01/11

(iii) Meta search engines	
Google/Google Scholar	
Intute	
SUMsearch	
TRIP	

Appendix 2

Topic: Cervical screening
Search question: ***To identify studies that describe the benefits and harms of changing cervical screening frequency from 3 year to 5 years in women aged 50 years or older. These could included cervical cancer incidence, cervical cancer mortality or morbidity, anxiety, cost effectiveness and coverage.***
For : Dr Sharon Hillier, Screening Division
By: Sian King, LKMS Swansea
Date : 31/01/11
Updated:

1.Methodology	
Search terms :-Keywords, Free text	Cervical screening Age$ adj4 50 Over 50$ Interval$
Database subject headings:- MESH, HMIC	Cancer invasion/di, pc Cancer screening Carcinoma squamous cell/di, pc Cervical cancer Cervical cancer-prevention and screening Cervical intraepithelial neoplasia Cervical screening Cervix neoplasms, Cervix uteri/ab Cervical cytology

	Mass screening Papillomavirus infections Screening Screening programmes Screening services Squamous cell carcinoma Uterine cervical neoplasms Uterine cervix Uterine cervix cancer Uterine cervix carcinoma Uterine cervix carcinoma in situ Uterine cervix tumor Uterus cancer Vagina smear Vaginal smears Age distribution Age factors Age of onset Early diagnosis Early detection of cancer Elderly : Screening Women Age Aged Middle age Middle aged Middle aged (45+ years) Older people

	Over 50s Anxiety Distress Costs Costs and cost analysis Cost benefit analysis Cost savings Cost effectiveness Cancer risk High risk population Risk factor Risk factors Target setting Time Time factors Data Incidence of disease Incidence Statistical data Tabular data
Limits	
• Publication types	Guidelines, reviews, reports, articles
▪ Language	English
▪ Dates covered	2000-2011
▪ Geographical location	Worldwide (developed countries)
Other criteria	

Filters	

2. Sources	
(i) Core databases/sources	
BNI	01/02/11
CINAHL	02/02/11
Clinical Evidence	n/a
Cochrane Library	31/01/11
EMBASE	01/02/11
HMIC	31/01/11
MEDLINE	31/01/11
NICE	01/02/11
Library catalogue & knowledge base	31/01/11
PsycINFO	01/02/11
Public Health Wales Document database	

(ii) Topic specific databases, sources	
Databases	

Websites	
ACOG	01/02/11
AHRQ (US)	31/01/11
Department of Health	01/02/11
National Breast and Cervical Cancer Early Detection Program	01/02/11
NI Cancer Screening Programme	01/02/11
NHS Cervical Screening Programme	01/02/11
NHS Evidence – specialist collection	02/02/11
NHS National Services Division (Scotland)	02/02/11
RCOG	02/02/11

(iii) Meta search engines	
Google/Google Scholar	
Intute	
SUMsearch	
TRIP	

Clinical Practice Guidance for the Assessment of Young Women aged 20-24 with Abnormal Vaginal Bleeding

Background

A recent review by the Advisory Committee for Cervical Screening recommended no change to the age of commencing cervical screening and that the screening range would remain at 25-64 years.

This decision was based on the potential for more harm, through morbidity consequent to screening, than benefit achieved by preventing cervical cancer. It was recognised, however, that in the rare cases of cervical cancer which do occur in women younger than 25 years (around 50 per year, with 0-5 deaths). There is a delay in diagnosis in a significant proportion because of delayed pelvic examination following self-referral with abnormal bleeding. The explanation for these delays, which have been documented at 4-6 months in some cases, is that relatively common symptoms of abnormal vaginal bleeding may be attributed initially to dysfunctional bleeding, or related to oral contraceptive use. The ACCS recommended the development of clinical practice guidance, which would reduce the risk of a delayed diagnosis of cervical cancer, by identifying those women most at risk of cervical cancer.

The Size of the Problem

The number of women aged 20-24 years who develop cervical cancer is generally fewer than 50 cases per year and this will fall over the next 10 years as a consequence of the national HPV vaccination programme. By contrast abnormal vaginal bleeding is relatively common in this age group. It has been estimated from a general practice dataset in Scotland (unpublished) that postcoital bleeding is reported by around 1 in 600 women aged 20-24 per year. Intermenstrual bleeding is more common than this and it may be that 0.5-1% of women in this age present with abnormal vaginal bleeding each year. There are around 1.5m women aged 20-24 in England and it could, therefore, be estimated that 7,500 – 15,000 women per year will report abnormal vaginal bleeding. In practice the number could be larger than this.

Developing a Guidance for Clinical Practice

The cardinal symptom of cervical cancer in this age group is postcoital bleeding, but persistent intermenstrual bleeding, which is more common, also requires attention. The critical intervention in the diagnosis of cervical cancer is an immediate speculum examination as recommended by SIGN2 and NICE3 Guidance, to enable a clear view of the cervix. Following a relevant history, it is, therefore, necessary for women who present with postcoital bleeding or persistent intermenstrual bleeding to be offered a speculum examination either in primary care or at a GUM clinic. This could be performed by a practice nurse experienced in cervical screening.

If the cervix looks abnormal and suspicious, which will be the case in a very small proportion, the correct action is urgent referral to colposcopy under the ‘two week wait’ rule. If there is a benign lesion, such as cervical polyp, a routine gynaecological referral will suffice. If the cervix looks normal, the recommended action will be a pregnancy test and testing for cervical infection (e.g. Chlamydia, N Gonorrhoea, Herpes), which could be performed in general practice, family planning clinics or GUM clinics. Any positive tests for sexually transmitted infections would need to be appropriately treated.

This pathway is illustrated below.

The impact of this guidance will be monitored by the Advisory Committee for Cervical Screening.

NHS Cancer Screening Programmes produce *Cervix chart for sample takers in primary care*, with pictures of the cervix showing various abnormalities. Copies of the chart can be ordered from www.orderline.dh.gov.uk, quoting NHSCSP publication No 25.

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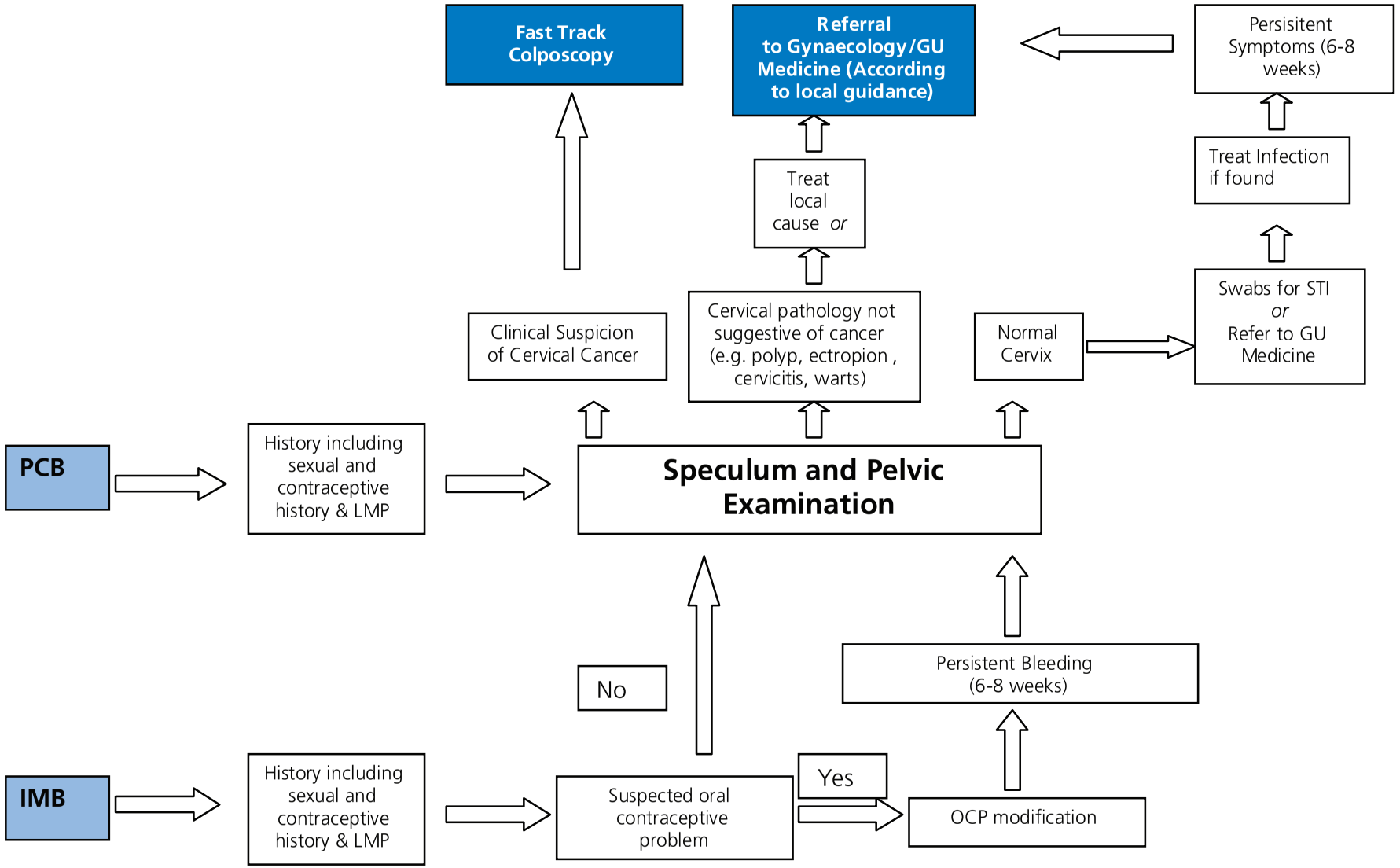
This guidance was developed by a working Subgroup of the Advisory Committee on Cervical Screening:

HC Kitchener	(ACCS Chair)
C Sonnex	(ACCS, GUM)
J Butler	(DH, Gynaecology)
S Firth	(ACCS, GP)
K Moss	(ACCS, GP)
M Shafi	(ACCS, Gynaecology)
P Walker	(Invited member, Gynaecology)



PCB – post coital bleeding
IMB – intermenstrual bleeding
LMP – last menstrual period

OCP – oral contraceptive pill
GU Medicine – Genitourinary medicine
STI – Sexually transmitted infection

Age of first invitation for Cervical Screening and frequency of invitation for women aged between 50-64years
UK NSC policy review

DRAFT 4

Background

UK policy on age of commencement and frequency for cervical screening is varied. England and Northern Ireland start at age 25 while Wales and Scotland at age 20. The UK National Screening Committee (UK NSC) has been asked by the Wales Screening Committee to produce a definitive UK NSC policy.

This document is a summary of reviews produced for all four UK countries and I am grateful to the authors for allowing us to quote directly from their reports.

Introduction

The aim of cervical screening is to reduce the incidence, and morbidity and mortality from invasive cervical cancer.

The current cervical screening policy for Wales is that women aged 20-64 years are invited for screening every three years. The policy in Scotland is to invite women aged 20-60 years every three years. In 2003, England changed policy to invite women every three years for those aged 25-49 and every five years for those aged 50-64. The decision for increasing the first age of invitation was based on a case control study published in 2003, which concluded that screening was less effective for young women.[1] Also there were concerns that because many young women had cellular changes that resolved spontaneously, screening could lead to unnecessary treatments, which could be a factor in premature delivery of subsequent pregnancies.[2]

The English cancer screening programmes decision to amend national policy for screening women aged 50-64 was based on results from the case control study published in 2003 which concluded that five yearly screening offered similar protection to three yearly in this older age group.[1] In July 2010 Northern Ireland announced that they would change to the same policy as England from January 2011.[3]

The decision to change the age of invitation has been controversial and there has been a lot of public and press interest. This was heightened following the publicity around the death of Jade Goody, a celebrity who died from cervical cancer in 2009, aged 27. Following campaigns to lower the screening age from Jo's Trust and others, the Department of Health in England asked its Advisory Committee on Cervical Screening (ACCS) to review the evidence. This was to ensure that the policy on starting screening at age 25 remained in the best interests of young women and was based on the latest available clinical evidence. The review took place at an extraordinary meeting of the Department of Health Advisory Committee on Cervical Screening in May 2009 and concluded that the starting age of screening should remain at age 25.[4]

Cervical Cancer

Natural History

Cervical cancer is caused by Human Papillomavirus (HPV) which is a sexually transmitted infection. Persistent infection by high-risk HPV types is detectable in more than 99% of cervical cancers. [5] The majority of high-risk HPV infections are transient and cause no clinical problems. Within one year, around 70% of new infections will clear and approximately 90% of new infections will clear within two years.[6,7] However, persistent infection by a high-risk HPV type is the most important causal factor for the development of cervical neoplasia.

Cervical intraepithelial neoplasia 1 (CIN 1) is a histologic diagnosis associated with benign viral replication and in most cases spontaneously regresses. Studies in adult women show regression rates of 70-80% whereas in adolescents and young women they show more than 90% regression.[8]

Cervical intraepithelial neoplasia 2 (CIN 2) is a lesion which in some cases may progress to cancer, although many of these are known to regress. The annual regression rate of CIN 2 in adult women is estimated to range from 15%-23% with up to 55% regressing by 4-6 years.[8]

Cervical intraepithelial neoplasia 3 (CIN 3) has the greatest potential to progress to invasive cancer at the rate of 0.2% to 4% within 12 months. Progression times from CIN 3 to invasive carcinoma vary between 5 to 19 years. [9,10,11]

Risk Factors

The risk factor for getting cervical cancer is persistent infection with high risk HPV. Smoking may increase the persistence of the virus: and having sexual intercourse at a young age, having many sexual partners and not using condoms increases the risk for getting HPV.

Age of first invitation for Cervical Screening

In order to inform the individual country based policies literature syntheses have been produced. Appended here are the reviews carried out for the English cancer screening programmes by Peter Sasieni, Alejandra Castañón, and Jack Cuzick from the Wolfson Institute of Preventive Medicine. The BMJ also published the finding of a review done by the English cancer team soon after. [12] An unpublished review from Cervical Screening Wales, Public Health Wales is also attached.(Appendix 1)

Benefits and harms of screening women between 20 and 25 years

Screening programmes should deliver more benefit than harm at a population level. The benefits of screening women aged between 20 and 25 years would be to identify cellular abnormalities that potentially could develop into cervical cancers; and to identify any cervical cancers that have already developed.

The harms of screening women this age are that normal cellular cervical changes in younger women may appear to be abnormal changes, leading to unnecessary treatment and potential anxiety for the woman. In some cases, treatment my lead to pre term delivery.

Number screened, number treated and number helped

A flow chart to show the numbers invited, referred and treated is appended in Appendix 2

Outcome data for Wales shows that for the cohort of women aged 25 years as of 1st February 2011 (n=20,225) and invited to screening from age 20 years, there were 1,774 referrals following an abnormal smear results and 949 referrals resulting in treatment. In this cohort there were 522 cases of CIN3, 16 CGINs and 7 cancers diagnosed.

Anxiety

It is reported in the literature that women who receive an abnormal smear result have increased anxiety, and their worries include fear that they have cancer, self blame, sexual guilt and concerns about infertility[13]. Most research has been on high grade abnormal smears however a study looking at 3500 women recruited to Tombola (trial of management of borderline and other low grade abnormal smear) found that women reported anxiety levels for low grade abnormal smear results which were consistent with those found in previous studies of women with high grade abnormal smear results. Stratification of the effect of age on anxiety was not discussed in any of the identified studies. But it is known that borderline and low grade abnormalities are found in higher proportions in younger women, so anxiety created by those conditions is likely to be more prevalent in younger women participating in screening than in an older population

Also there were no studies identified that discussed the effect of different policies across the UK on age of invitation, as young women may have been anxious especially following media attention on the death of a celebrity from cervical cancer.

Premature birth

The relation between cervical cancer treatment and pre-term delivery has been debated. The following is from the Welsh report and summarises the position. For women in this age group there is concern about the possible impact on colposcopic interventions for future pregnancies. In a critical review of the literature published by the NHS Cervical Screening Programme[17] conflicting results from studies were reported. In 2007 a systematic review and meta analysis[14] of 27 studies found that LLETZ was significantly associated with preterm delivery with an overall Relative Risk of 1.70 (95% CI 1.24 - 2.35). In the five further primary research studies conducted after the meta analysis four

found that treatment was associated with an increased risk of preterm delivery and one found that the diagnosis of CIN3 was associated with preterm delivery and not treatment itself[15]. The majority of studies have been limited in their ability to take into account potential confounding factors that could be independently associated with being referred for colposcopy and preterm delivery for example maternal smoking, socioeconomic status and previous obstetric history.

Frequency of screening for women aged 50 to 64 years

The screening interval for a screening programme needs to be based on the natural history of the disease in that population.

The evidence on which the screening interval was based was originally an international study conducted by the IARC that estimated yearly screening reduced the incidence of invasive cervical cancer by 94%, three yearly by 91%; five yearly by 84% and 10 yearly by 64%. [16] In 2003 two studies were published which provided more evidence on screening frequency. The first paper [1] analysed screening histories of 1305 women aged 20-69 years, diagnosed with frankly invasive cervical cancer and 2532 age matched controls obtained from the UK screening programme database. Their analysis showed that by using time since the last operationally negative cytological smear 4.5 to 5.5 yearly screening offered 72% (95% CI 43%-86%) protection compared to 2.5-3.5 yearly screening protection of 85% (95% CI 74%-92%) for women aged 55-69 for frankly invasive cervical cancer.

The authors produced summary point estimates of protection and concluded that five yearly screening offered similar protection to 3 yearly. The results of this paper informed England's decision to standardise to inviting women aged 50-64 years every 5 yearly. This paper has age groups in 55-69 and the policy is 50 -64 to allow time from screening to cancer diagnosis. The issues are that the paper assumed that screening to cancer diagnosis does not vary by age from 50 to 55 years, the analysis did not include screen detected micro invasive cancers; there were 490 (18%) results that had cancer stage unknown which may have biased the results, and the data was from England and the population in Wales may be different.

A Dutch study published in 2004[17] supported a five year screening interval by reporting that the incidence of squamous cell carcinoma and precursor lesions remained stable when changing from a 3 year to 5 year screening interval. However this study did not stratify the results by age.

Unpublished work undertaken by Sasieni *et al* and Cervical Screening Wales explored the effectiveness of the screening programme in Wales between 1999 and 2007. The odds ratio for screening between 1990 and 2001 were compared to those between 1999 and 2007 and population attributable risks were calculated. A total of 1,466 cases of cervical cancer were diagnosed in Wales between 1999 and 2007, 73% of which were diagnosed in women aged 20-64 years. There was no evidence to suggest that extending the screening interval from 3 yearly to 5 yearly in women aged over 50 years increased the risk of developing cervical cancer (0R 0.17, 95% CI 0.11- 0.27 vs, OR 0.14 95% CI 0.08-0.24 respectively).

HPV

The NHS Cervical Screening Programme in England will begin incorporating HPV triage and Test of Cure into their screening programme this year. The sentinel site implementation project tested samples from women which contained cells with low-grade abnormalities (borderline or mild dyskaryosis). If they tested positive for high-risk HPV strains the women were referred for colposcopy and if they were negative for high risk HPV strains the women could be returned to routine recall.

The Scottish group convened to discuss the issue agreed to recommend that the lower age for screening in the Scottish Cervical Screening Programme be increased from 20 to 25. It was considered prudent to delay this increase in the lower age range until the HPV school vaccination programme is fully implemented and so implementation should be fully completed by 2015.

Summary

That the UKNSC recommend that

- The age of first invitation for cervical screening be raised to 25 in Wales and Scotland on the basis that there is evidence of a large number of women screened and treated with relatively little benefit below this age.

- Screening for women aged 50-64 is undertaken five yearly.

Anne Mackie September 2012

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[17] Siemens FC, Boon ME et al Population-based cervical screening with a 5-year interval in the Netherlands. *Acta Cytolgica* 2004 **48** 348-54

UK National Screening Committee (UK NSC)
Note of the meeting held on 13 November 2012
at
The Scottish Government, Room 4ER, St Andrew's House,
Regent Road, Edinburgh, EH1 3DG

Present
Sir Harry Burns (Chair)
Dr Eric Baijal
Dr Margaret Boyle
Mrs Clare Brassington
Ms Alison Brown
Dr Catherine Calderwood
Professor Alan Cameron
Dr Jennie Carpenter
Professor Gareth Evans
Dr Rosemary Fox
Dr Nick Hicks
Mrs Madeleine Johnson
Mr Nick Johnstone-Waddell
Dr Surendra Kumar
Dr Janet Little
Dr Anne Mackie
Dr Gordon Paterson
Ms Cheryl Paris
Dr Heather Payne

Visitors
Mr Tim Elliott (by tele-conference)
Miss Laura Grainger
Mr John Marshall
Professor Catherine Peckham
Professor Robert Steele

Secretariat
Miss Jo Taylor
Miss Kathryn Flynn

Apologies
Ms Alex Berry
Dr Sunil Bhanot
Professor Roger Brownsword
Professor Martin Buxton
Ms Majella Byrne
Dr David Elliman
Ms Jane Fisher
Mrs Moira Morris
Professor Julietta Patnick
Dr David Walker

Welcome and Introductions

1.0 Sir Harry Burns welcomed all to the meeting including:-

New UK NSC Members

- Dr Eric Baijal, Joint Director of Public Health, NHS Borders who will be replacing Dr Lesley Wilkie on the committee.
- Ms Alison Brown, who will be giving a consumer's perspective on screening to the committee.
- Dr Heather Payne who will be replacing Dr Jane Wilkinson as the Welsh Government's representative on the committee.

Agenda Item Presenters

- Professor Catherine Peckham CBE, Programme Director, NHS Infectious Diseases in Pregnancy Screening Programme, presenting the antenatal screening for Human T-Cell Lymphotropic Virus-1 agenda item.
- Mr John Marshall, UK NSC Projects and Programmes Manager, presenting the antenatal screening for group B streptococcus carriage, antenatal screening for feto-maternal alloimmune thrombocytopenia and newborn screening for kernicterus agenda items.
- Professor Robert Steele, University of Dundee and Mr Tim Elliott, Cancer Policy Team, Department of Health, presenting the bowel screening using flexible sigmoidoscopy agenda item.

Observer

- Miss Laura Grainger, shadowing Miss Josephine Taylor as part of the NHS Management Programme.

2.0 Minutes and Matters arising

2.1 The minutes of the last meeting were agreed.

2.2 There were ten actions points from the last meeting. Most were picked up as main agenda items. In addition:

1.2 Vacancies

Ms Alison Brown had been appointed as the consumer representative on the committee.

4.12 Draft policy for HPV testing to alter follow up regimes in cervical cancer

The draft policy for Human Papilloma Virus (HPV) testing to alter follow up regimes in cervical cancer paper will be placed on the UK NSC website for consultation shortly.

4.12 Draft policy for HPV testing to alter follow up regimes in cervical cancer

The draft policy for HPV as Primary Screen for Cervical Cancer paper will be placed on the UK NSC website for consultation shortly.

4.24 Bowel Cancer Screening

The evaluation of the 'Be Clear On Cancer Campaign' will be brought to a future meeting.

4.30 Bowel Cancer Screening

An evaluation of the faecal immunochemical test against the UK NSC criteria will be a future agenda item.

5.20 Asymptomatic Bacteriuria Screening in Pregnancy Policy Position Statement

Mr John Marshall will write to the National Institute for Health and Clinical Excellence (NICE) and the Health Protection Agency (HPA) about the issues identified in the asymptomatic bacteriuria screening in pregnancy review shortly.

5.35 Screening for Duchenne Muscular Dystrophy Policy Position Statement

Mr John Marshall will write to the All Party Parliamentary Group on Muscular Dystrophy shortly.

3.0 Director's Report Back

3.1 Dr Mackie gave an update as follows:-

Update on Newborn Screening for Maple Syrup Urine Disease (MSUD), Homocystinuria (pyridoxine unresponsive), Glutaric Aciduria Type I (GA1), Isovaleric Acidaemia (IVA) and Long-chain 3 - hydroxyacyl CoA dehydrogenase deficiency (LCHADD)

3.2 The evaluation to investigate extending the Newborn Bloodspot Screening Programme to include the above five conditions began in July 2012. While the evaluation takes place screening is offered to the populations served by the screening laboratories in Leeds, Manchester, Sheffield, Birmingham, London (Guy's and St Thomas' and Great Ormond Street). The evaluation would end on 19 July 2013, however, funding has been secured to extend screening for the above conditions for a further year while data is collected, analysed and written up. To date there have been ten test positive results with five children receiving a screening positive result after further investigation. The completed evaluation will be brought back to a future meeting for discussion.

Action: Dr Mackie to bring the completed evaluation to a future meeting

Pulse Oximetry Screening for Critical Congenital Heart Defects

3.3 Pulse oximetry is a well established, accurate, non-invasive test for objective quantification of hypoxaemia in sick babies. Recent studies (referenced in the UK NSC paper) have addressed the accuracy of pulse oximetry as a screen for critical congenital heart defects (CCHD) and further recommend this as an addition to the current screening in the antenatal and newborn screening programmes.

3.4 An evaluation of the extent of the value and cost effectiveness of including a pulse oximetry test in the NIPE Screening Programme concluded that given the significant mortality and morbidity impact of undiagnosed CCHD this was likely to be quite cost effective. However, uncertainty remained about the best way of incorporating pulse oximetry into the clinical examination.

3.5 The NIPE Programme Centre had worked with a clinical reference group to document a best practice pathway that includes pulse oximetry and will be consulting on the pathway over the next few months.

3.6 Members asked who would carry out the pulse oximetry test and whether there would be staffing implications for neonatal care departments. Dr Mackie said it was envisaged that midwives or NHS hearing screeners could carry out the test. She said the consultation on the pathway should help determine who should carry this role out and highlight any potential staffing problems.

3.7 The completed review of pulse oximetry screening for CCHD will be brought to the next meeting.

Action: Dr Mackie to bring the pulse oximetry screening for CCHD review to the next meeting

European Council Recommendation on Rare Diseases

3.8 Dr Mackie informed members that the United Kingdom Plan for Rare Diseases consultation which closed in May had asked respondents to consider whether the UK NSC should take into account the benefit of screening in reducing the 'diagnostic odyssey' and in allowing informed choice for subsequent family planning. A copy of the summary of consultation responses to the question on screening had been shared in confidence with the UK NSC.

3.9 Members discussed the consultation responses included in the paper. Members were concerned about responses which suggested the UK NSC lacked transparency and appropriate patient representation. Members asked for it to be made clear that the UK NSC has a clear policy review process (http://www.screening.nhs.uk/policyreview), all policy reviews follow this process and involve a three month public consultation. Guidance entitled 'Engaging with the UK NSC's policy review process' has been produced for stakeholder groups, explaining the policy review process and how to make effective submissions to policy consultations. Patient and lay representatives are represented on the UK NSC, Fetal, Maternal and Child Health Co-

ordinating group and on all NHS Screening Programme advisory and steering committees such as the Bloodspot Screening Advisory Group in England.

3.10 Consultees had raised concerns about the lack of randomised controlled trials for rare diseases. The UK NSC's internationally recognised criteria for appraising the viability, effectiveness and appropriateness of a screening programme states that there should be evidence from high quality RCTs that the screening programme is effective in reducing mortality or morbidity. The UK NSC acknowledges that undertaking RCTs is problematic in some areas and acknowledges that evaluations such as the one currently taking place on newborn screening for MSUD, Homocystinuria (pyridoxine unresponsive), GA1, IVA and LCHADD could be used as evidence where RCTs are not feasible.

3.11 Members agreed that the current criteria allow for consideration regarding time to diagnosis. They further agreed that in the case of rare diseases reviewers of screening policy should take into account reduction of the diagnostic odyssey. Members felt that the rights of children and young people should be addressed when looking to answer these questions. Members agreed that when reviewing screening programmes against its criteria consideration of the value placed on the benefit and disbenefits should be clear and stated in the review of evidence.

4.0 Fetal Maternal and Child Health Screening

Report from Fetal, Maternal and Child Health Co-ordinating Group

4.1 Mrs Madeleine Johnson, Chair of the Fetal, Maternal and Child Health Co-ordinating Group (FMCH) said that there had been two meetings of the FMCH since the UK NSC had last met. These took place in July and November. The paper circulated to the UK NSC related to the July meeting only. Mrs Johnson reported that:-

Policy review work

4.2 Reviews for a number of conditions discussed at the July meeting of the FMCH are main agenda items for today's meeting. At November's meeting it was agreed that changes needed to be made to the antenatal screening for syphilis review and newborn screening for biotinidase deficiency review before they could open for public consultation.

Newborn screening for sickle cell carriers

4.3 A review of newborn screening for sickle cell carriers in Wales concluded that screening for sickle cell carrier status in the newborn does not meet the UK NSC criteria for a screening programme. The Wales Screening Committee and the Newborn Bloodspot Project Board would work with the English Sickle Cell and Thalassaemia Screening Programme to explore the potential of TMS to detect sickle cell disease with and without detecting carriers.

NHS Fetal Anomaly Screening Programme (NHS FASP) 18 – 20 week standards

4.4 A project to update the programme standards is ongoing. As part of this concern had been raised that scanning within the current screening window has generated an increasing rate of repeat scans. The rate of repeat scanning appeared to vary by both gestation and unit. A proposal on an alternative screening window from NHS FASP is expected in March.

Second trimester serum screening for Trisomy 21(T21) using the quadruple test

4.5 There is currently no nationally recommended test for twin pregnancies presenting later than 14 weeks + 1 day. NHS FASP proposed extending the recommendation for singleton pregnancies, the quadruple test (maternal serum AFP, intact or free βhCG, inhibin A + oestriol), to the small group of women with twin pregnancies presenting in the second trimester. In discussions members said they would find it helpful if some of the Down's Syndrome Screening Quality Assurance Support Service's data could be published. More information on this issue was considered necessary and an updated paper is expected to be presented to the FMCH in March.

Screening for T13 & T18

4.6 A review in this area is currently being commissioned in collaboration with NHS FASP.

Screening for Tay Sachs Disease, Canavan Disease and Familial Dysautonomia

4.7 Solutions for Public Health reviewed the evidence for antenatal, newborn and adult carrier screening for the above three conditions earlier this year. The documents were available for consultation for three months from May 2012 on the UK NSC website. The consultation responses raised a number of complex issues and the FMCH felt it would be appropriate to hold a workshop in the new year to consider the issues raised by the reviews and the consultation responses prior to making a policy recommendation to the UK NSC.

Rubella Susceptibility Screening in Pregnancy

4.8 At the last UK NSC meeting members had agreed that screening for rubella susceptibility does not meet the UK NSC criteria for a screening programme. The UK NSC had agreed that the present arrangements for antenatal screening and post partum immunisation should continue until other arrangements are in place. The Joint Committee on Vaccination and Immunisation has agreed to work jointly with the UK NSC to look at alternative approaches to screening.

4.9 Members noted the FMCH update.

Antenatal Screening for Human T-Cell Lymphotropic Virus (HTLV-1) Policy Position Statement

4.10 Professor Catherine Peckham presented this item. HTLV-1 screening had previously been reviewed in 2003 and the recommendation was that screening should not be offered. HTLV-1 infection is life-long and most infected individuals remain asymptomatic. However, after a long latent period a small but significant proportion of individuals infected with HTLV-1 develop serious neurological and lymphoproliferative disease.

4.11 Members discussed the consultation replies. Responses had been received from the HTLV Patients Forum and the National HTLV clinical service, the National Centre for Human Retrovirology based at St. Mary's Hospital NHS Trust. While both were critical of the review and its conclusion, much of the review's content was accepted.

4.12 The UK NSC agreed the policy position on antenatal screening for HTLV-1 as a national antenatal screening programme for HTLV-1 is not recommended because:

- The prevalence of infection is very low in the UK with limited data on prevalence in the defined risk groups
- The risk of mother-to-child transmission is low and data on the long term consequences of infection lacking
- There is no effective treatment
- The impact of avoiding breastfeeding is uncertain
- The negative impact of maternal diagnosis of HTLV-1 on the woman and her family must not be underestimated

4.13 The UK NSC agreed that the policy should be reviewed in three years' time unless there is significant new peer reviewed evidence in the meantime.

4.14 The UK NSC agreed that the National Centre for Human Retrovirology should be encouraged to approach specialised commissioners regarding work in high risk groups / areas.

Action: Dr Mackie to write to the National Centre for Human Retrovirology

Antenatal Screening for Group B Streptococcus Carriage Policy Position Statement

4.15 Mr Marshall introduced this item. The last review in 2009 concluded that screening for group B streptococcus (GBS) carriage should not be offered to all pregnant women. The latest review undertaken by Bazian concluded that the evidence had not changed significantly in key areas. These included:

- the natural history of transmission of GBS from the intestine and the genital tract to the baby is poorly understood

- the rate of early onset GBS in the UK is comparable to those countries in which screening is recommended and benefits of screening are uncertain
- screening at 35 - 7 weeks will not impact on a significant burden of early onset GBS disease
- the test cannot distinguish between the majority of low risk women and the minority whose baby will be affected, this results in over-detection and over-treatment of a very large number of women at very low risk.

As such a change of policy was not recommended.

4.16 Mr Marshall said that the flow chart contained in the papers estimated that the introduction of a screening programme would prevent 5 -7 deaths in the newborn per year and between 17,000 - 25,000 women would receive antibiotics in labour to prevent 1 death. The consequences of expanding the use of antibiotics are unknown and there was concern about the long term effects on the newborn and the potential for anaphylactic reactions in labour.

4.17 In discussion members were clear that the loss of any baby was devastating and acknowledged that this came through clearly in the consultation responses. Members were concerned about the use of antibiotics. A submission to the consultation from Northern Ireland reported an audit in which there had been two confirmed cases of maternal anaphylaxis from penicillin during labour, one of whom died. A third case, thought to be an anaphylactic reaction had yet to be confirmed. Research interest was focusing on the long term effects of antibiotics on the newborn such as obesity and asthma. Members felt that the practical impact screening would have on the antenatal and postnatal pathway was an important dimension which did not come through fully in the review as it was not explored in the published literature.

4.18 Mr Marshall drew attention to the consultation responses, in particular the response from Group B Strep Support Group (GBSS). The group were concerned that the UK NSC is biased in its review and treatment of this issue, in particular that the UK NSC had not used a systematic review methodology. Members were clear that the methodology was consistent with that used for other screening reviews considered acceptable to stakeholders. Systematic reviewing in this context would have slowed down the process and incurred costs that couldn't be justified by the knowledge that would potentially be gained. Members did, however, agree that it would be helpful to expand the information on the UK NSC website on the methodology.

4.19 On the review process, members agreed that this had also been consistent with the publicised process and with many other reviews undertaken by the UK NSC. The consultation process was transparent, had taken account of a large number of publications including that supplied by GBSS and other stakeholders and there had been extensive consultation (including experts recommended by GBSS). The review had been consultative and that it had tried to incorporate the views of stakeholders where possible.

4.20 Following extensive discussion members agreed that the current policy should be retained. This is because there is insufficient evidence to demonstrate that the benefits to be gained from screening all pregnant women and treating those carrying the organism with intravenous antibiotics during labour would outweigh the harms. Members were however, unanimous in their view that action needs to be taken to improve the outcome for babies affected but until a more effective test could be found screening did not provide the tool to do this.

4.21 Members also considered that the paper was complicated and policy position statement was quite technical. It was agreed that work should be undertaken to simplify the terminology to make it easier to understand from a lay perspective. An accompanying Q&A would be helpful in this respect.

Action: Mr Nick Waddell to produce Q&A and publish it on the UK NSC website

4.22 Members also agreed that the following text should be added to the policy statement:

"The current UK rate of early onset GBS is comparable to that in countries in which screening is recommended. A significant burden of disease is found in risk groups whose management would not be affected by a screening programme. The ability of screening to significantly impact on mortality and long term morbidity caused by GBS is uncertain.

Systematic reviews of culture testing suggest that many screen positive women may no longer be carriers at the point of treatment. In the absence of a diagnostic test, current screening strategies are unable to distinguish between carriers whose babies will be affected by early onset GBS and those which would not. As a result many thousands of low risk women would receive intravenous antibiotic prophylaxis during labour. The consequences of expanding antibiotic usage in this way are unknown."

4.23 A range of further follow up action was agreed for exploration with key stakeholders:

- the Director of Programmes' office should work to develop a communications strategy to promote understanding of the policy, perhaps in collaboration with the Royal College of Obstetricians and Gynaecologists and NICE;
- a detailed modelling exercise based on assumptions arising from the review could be considered;
- a national surveillance study should be encouraged to generate up to date epidemiological data;
- a review of issues relating to antibiotic use in pregnancy and labour should be commissioned given the evolving context of work on the microbiome and the National Perinatal Epidemiology Unit's study of anaphylaxis in pregnancy and labour;
- the possibility of natural history studies exploring vertical transmission of GBS and development of early onset GBS in the newborn;

- work should be undertaken with the HTA to explore the possibility of studies of rapid testing in high risk groups (for example prolonged rupture of the membranes or preterm deliveries) as a means of targeting antibiotics in these populations.

Action: Dr Mackie to contact stakeholders about these actions

Antenatal Screening for Feto-Maternal Alloimmune Thrombocytopenia (FMAIT) Policy Position Statement

4.24 Mr Marshall presented this item. The previous review had recommended that screening should not be offered. Mr Marshall said screening would aim to prevent severely affected cases (eg intracranial haemorrhage and intrauterine fetal death) in first affected pregnancies.

4.25 Members discussed the consultation responses. Mr Marshall said a positive endorsement of the review and its conclusions was received from the British Committee for Standards in Haematology. Detailed comments were received from the NHS Blood and Transfusion Service and the National Perinatal Epidemiology Unit. Comments from these organisations had been taken account of in the review following consultation.

4.26 The UK NSC agreed the policy position on antenatal screening for FMAIT as a national antenatal screening programme for FMAIT is not recommended because:

- The incidence of the FMAIT, as a whole, is unclear and in addition the incidence of severely affected cases is unclear.
- There is uncertainty about the long term clinical effects of FMAIT.
- A suitable predictor of severely affected cases had not been identified and, consequently, a test which could identify pregnancies which would benefit from intervention was lacking.
- There is a lack of a clear management strategy for anti HPA-1a women

4.27 The UK NSC agreed that the policy should be reviewed in three years' time unless there is significant new peer reviewed evidence in the meantime.

Newborn Screening for Kernicterus Policy Position Statement

4.28 Mr Marshall presented this item. He stated that kernicterus is a very rare complication of neonatal unconjugated hyperbilirubinaemia. In kernicterus high levels of bilirubin cause brain damage leading to neurological symptoms such as hearing loss and cerebral palsy and can in some cases be fatal. Screening for hyperbilirubinaemia has been suggested as a means of preventing kernicterus. The UK NSC previously reviewed screening for kernicterus in 2006. More recently the US Preventive Services Task Force considered the condition in 2009 and concluded that there was insufficient evidence on the benefits and harms of screening to recommend its introduction.

4.29 NICE had published guidance on the management of jaundice and this recommends an approach to testing babies' bilirubin levels based on risk factors. These being: prematurity (<38 weeks), sibling with jaundice requiring phototherapy, maternal intention to breastfeed exclusively, jaundice in first 24 hours of life.

4.30 Members discussed the consultation responses. The responses received agreed with the screening review's provisional recommendation.

4.31 The UK NSC agreed the policy position on newborn screening for kernicterus as a national newborn screening programme for kernicterus is not recommended because:

- There is an uncertain correlation between hyperbilirubinaemia and bilirubin encephalopathy. The association is often mediated by underlying problems such as blood group / rhesus incompatibility, infection, G6PD deficiency. More generally the progression from raised bilirubin levels to kernicterus is not well understood. Some babies develop bilirubin encephalopathy without having hyperbilirubinaemia and some with severe hyperbilirubunaemia do not develop bilirubin encephalopathy.
- There appears to be some good evidence that babies at risk of developing hyperbilirubinaemia can be reliably detected using risk factors and /or bilirubin measurement. But as a marker of risk these appear insufficient in predicting bilirubin encephalopathy.
- There is insufficient evidence that phototherapy is effective in treating hyperbilirubinaemia with the aim of preventing severe hyperbilirubinaemia.

4.32 The UK NSC agreed that the policy should be reviewed in three years' time unless there is significant new peer reviewed evidence in the meantime.

Screening for Autistic Spectrum Disorders in Children Under 5 Policy Position Statement

4.33 Dr Mackie presented this item. Dr Mackie said autism spectrum disorders (ASD) are complex developmental disorders, including autism, Asperger's syndrome and pervasive developmental disorders. The previous screening review had concluded that screening for autism should not be offered. Dr Mackie said Solutions for Public Health were asked to review publications from January 2005 – November 2010 for the current review. The review focused on issues relating to the test and the treatment.

4.34 Members discussed the consultation responses. Dr Mackie said the review had been revised following consultation to reflect the comments received.

4.35 The UK NSC agreed the policy position on screening for autism and autistic spectrum disorders in children under 5 as a national screening programme for autism and autism spectrum disorder in children under 5 is not recommended because:

- Studies of the natural history of these conditions indicate that about a third of children who are given a diagnosis of 'autism' at 20-23 months of age as a result of a screening programme, and up to a quarter of those identified as being within the broader category of 'ASD', are likely to lose these diagnostic labels by the age of four years. It is not clear whether these figures reflect the impact of early intervention (assuming it is effective) or over-diagnosis at 20-23 months of age.
- No approach to screening for ASD has demonstrated reasonable performance, in terms of both sensitivity and positive predictive value, in a general population screening study.
- Approaches to screening for ASD used in recent studies are not accepted by a substantial proportion of parents. Parents of between one third and one half of all children who failed the initial screening test dropped out of the screening process before it had completed. Whether an established screening programme staffed by clinicians would be more acceptable than the approach used in these research studies is unknown.
- The review identified only three RCTs of Early Intensive Behavioural Intervention / Applied Behaviour Analysis, in which a total of 100 children have been studied.
- The effect of early intensive behavioural intervention/applied behaviour analysis on outcomes varied across the three identified RCTs. The most consistent effect (in two RCTs) was an improvement in IQ. The duration of follow-up in the largest trial (Dawson et al 2010) was limited to two years.
- The review identified 11 RCTs of various focused behavioural interventions, most of which reported some benefit from intervention. However, only one of these studies involved more than 60 children, and in most of them the children were followed up for only one year or less.
- Whether the short-term effects reported in these RCTs lead to significant improvements later in childhood, or greater independence and improved vocational and social functioning in adulthood, is unknown.

4.36 The UK NSC agreed that the policy should be reviewed in three years' time unless there is significant new peer reviewed evidence in the meantime.

Adolescent Idiopathic Scoliosis Screening Policy Position Statement

4.37 Dr Mackie presented this item. The purpose of screening for AIS is to identify a cohort of children who would benefit from interventions to reduce progression to clinically significant scoliosis and to reduce the need for spinal surgery. The UK NSC last reviewed screening for scoliosis in 2006 and recommended that screening should not be offered.

4.38 Members discussed the response to the consultation from the Scoliosis Society.

4.39 The UK NSC agreed the policy position on screening for scoliosis as a national screening programme for scoliosis is not recommended because:

- The accuracy of the most commonly used test, the forward bend test, and its ability to predict progression to clinically significant scoliosis is

questionable. As the test is unable to consistently identify a group of children who would progress in this way, screening could lead to unnecessary follow up procedures such as x-ray with which harm is associated. Scoliosis requiring aggressive treatment is likely to be detected without screening.

- The treatment usually involves exercise, bracing and surgery or a combination of these approaches. In general, there was some evidence to suggest that these approaches in adolescence lead to health benefits in only a small proportion of cases. As the majority of screen detected cases would not progress to clinically significant scoliosis, screening could lead to unnecessary referrals and treatment.

4.40 The UK NSC agreed that the policy should be reviewed in three years' time unless there is significant new peer reviewed evidence in the meantime.

5.0 Adult Screening

Prostate Cancer Screening

5.1 Dr Mackie presented this item. Following the UK NSC meeting on 25 April 2012, Dr Mackie had asked the School of Health and Related Research (ScHARR) to re-calibrate their disease model to include the latest European Randomized Study on Screening for Prostate Cancer (ERSPC) results and other relevant literature of the effect of screening for prostate cancer on the incidence of prostate cancer and prostate cancer mortality. Dr Mackie had also requested an update of key parameters in the screening model (for example adverse events of treatment, utility values, costs) where there is significant new data.

5.2 Dr Mackie said ScHARR are currently in the process of redesigning the model as a cohort model of disease natural history. She also reported that ScHARR have carried out six searches for literature to inform the model parameters. ScHARR had been unable to complete the work in time for this meeting.

5.3 A revised prostate cancer screening model would be brought to the next meeting of the UK NSC.

Action: Dr Mackie to bring ScHARR's revised prostate cancer screening model to the next UK NSC meeting

Bowel Screening Using Flexible Sigmoidoscopy

5.4 Mr Tim Elliott and Professor Robert Steele presented this item. Mr Elliott said following delays, the IT system to support the flexible sigmoidoscopy (FS) pilots in England is now under development, and is due to be delivered in March 2013, when the pilots will start. Having met all the criteria, six pilot sites have been identified. Up to 20 other sites have also been identified to become Wave 1 of roll-out sites from October 2013. The pilot and roll-out were therefore still on track to deliver the commitment of 60% coverage of FS screening across England by March 2015.

5.5 Professor Robert Steele gave a presentation on bowel screening in Scotland. A copy of the slides are available at Annex A. Professor Steele said that in Scotland men and women from the age of 50 are offered bowel screening using guaiac faecal occult blood testing (gFOBT). Professor Steele said following the UK NSC recommendation on 10 March 2011 that FS met the UK NSC criteria for a screening test, Scotland had been considering how and at what age to introduce FS. Professor Steele said funding had been secured to carry out either an evaluation or an RCT in Scotland on offering FS at around the age of 60 in addition to the current gFOBT screening programme.

5.6 Members discussed whether an evaluation or an RCT should take place. Members felt that more information could be gathered from an RCT and endorsed this approach. Professor Steele said the results of the RCT would be brought to a future meeting.

Actions: The Scottish Government to bring the results of the RCT to a future meeting

Breast Screening Review in England

5.7 Mr Elliott presented this item. Mr Elliott reported that an independent review of breast cancer screening in England was published on 30th October 2012, along with an accompanying paper in The Lancet. The panel consisted of nationally and internationally recognised experts in epidemiology and/or medical statistics as well as in current breast cancer diagnosis and treatment practices. No panel member had previously published on breast screening. The independent panel concluded that:

- *Relative mortality*
  The panel's best estimate is a 20% reduction in mortality from breast cancer in women invited for screening.

- *Absolute mortality benefit*
  Around one breast cancer death is prevented for every 200 women invited.

- *Over-diagnosis*
  Around 20% of the cancers detected through breast screening may not have been a problem in the lifetimes of the women invited for screening.

- *Lives saved*
  For the UK based breast screening programmes, the panel estimate that around 1,300 deaths are prevented each year (amounting to 22,000 years of life saved).

- *Balance of harms and benefits*
  For every 10,000 women invited for breast screening between 50 and 70 years old, the panel estimate that 681 cancers will be diagnosed of which129 will represent over-diagnosis, and 43 deaths from breast cancer

will be prevented. Thus three cases are over-diagnosed for every death prevented.

5.8 Mr Elliott said the Panel concluded that "the UK breast screening programmes confer significant benefit and should continue." However, the panel also said "It is now vital to give women information that is clear and accessible before they go for a mammogram so they can understand both the potential harms and benefits of the process".

5.9 Mr Elliott said the Panel's review of the randomised trials of breast screening lead to recommendations about future research priorities. These were included in the meeting paper.

5.10 Mr Elliott said that, in light of their findings on overdiagnosis, the Panel had recommended a re-evaluation of the cost-effectiveness of the NHS breast cancer screening programme. Dr Mackie said Professor Martin Buxton had expressed an interest in this work, and that she would be discussing how best to take this work forward with Professor Julietta Patnick and Professor Sir Mike Richards.

5.11 Mr Elliott said a group had been established to advise on the revision of information for invitees and promoting informed choice across all the cancer screening programmes in England. Members asked if the leaflets could be written in lay persons terms so people can easily understand them and that the same information be adopted in all four UK countries.

5.12 The UK NSC noted the update

Age of First Invitation for Cervical Screening and Frequency of Invitation for Women Aged Between 50 -64 Years

5.13 Dr Mackie presented this item. Dr Mackie said age of commencement and frequency of invitation of cervical screening varies across the UK. The age ranges offered screening in each country is as follows:

- Wales - women aged 20-64 years are invited for screening every three years
- Scotland - women aged 20-60 years are invited for screening every three years
- England - women aged 25 – 49 are invited for screening every three years and every five years for those aged 50-64
- Northern Ireland - women aged 25 – 49 are invited for screening every three years and every five years for those aged 50-64

5.14 Dr Mackie said the Welsh Screening Committee had asked the UK NSC for a definitive UK NSC policy on the age at which women should first be invited for cervical screening. Dr Mackie had carried out a screening review which had been open for consultation for three months from the 10 May 2012 until 10 August 2012.

5.15 Members discussed the thirty responses received to the consultation. The UK NSC received ten responses from NHS and professional organisations (mostly based in Wales). These organisations were supportive of the UK NSC's provisional recommendation. Of the seven responses from individual clinicians/professionals, one was supportive, five were not supportive and one didn't have a view. Concerns raised focused on the role of HPV vaccination and the need to consider the women who have not been vaccinated. The issue of increased sexual activity amongst young people was also raised as a reason to continue screening from 20, as well as the potential for sending mixed messages about the importance of early detection of cancer.

5.16 Three charities responded to the consultation. These were Cancer Research UK, Jo's Trust and the Mercedes Curnow Foundation. Cancer Research UK and Jo's Trust supported the UK NSC's provisional recommendation. The Mercedes Curnow Foundation did not agree with the provisional recommendation. They stated that some young symptomatic women are being missed as GPs are not always following the NHS clinical practice guidance. The ten individual members of the public who responded were critical of the recommendation, though there was some confusion about the purpose of offering screening and whether symptomatic women can or should receive a screening test. Other concerns expressed were that raising the age is just a cost-cutting exercise and that it is a violation of the human rights of women under 25 to deny them the choice of being screened. Members thanked all of the public who responded to the consultation, many of whom had shared their personal experiences with the UK NSC.

5.17 Dr Kumar asked whether there was any advice for GPs who received a request for a cervical screening test from a young woman under the age of 25 who was not symptomatic of cervical abnormalities. Mr Elliott said that the Advisory Committee on Cervical Screening in England had developed such guidance following the review of first screening age in England in 2009, which was available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_113478. The guidance has been endorsed by the Royal College of Obstetricians and Gynaecologists, the Royal College of General Practitioners and the Royal College of Physicians.

5.18 The UK NSC agreed the policy position on screening for cervical abnormalities as a national cervical screening programme is recommended. The age of first invitation for cervical screening should be raised to 25 in Wales and Scotland on the basis that there is evidence of a large number of women screened and treated with relatively little benefit below this age. Screening for women aged 50-64 should be undertaken five yearly.

5.19 Members stated that if the Welsh Government and the Scottish Government accept the UK NSC's recommendation public awareness campaigns need to be put in place to ensure people find out about and understand the reasons for the changes to the cervical screening programmes.

6.0 Updates (for information)

These are for information only.

6.1 MRC trials administered by Efficacy and Mechanism Evaluation (EME) Programme

6.2 HTA Update

6.3 SIGN Update

7.0 Any Other Business

There was none.

8.0 Next Meeting

Wednesday 20th March 2013
11:30am – 3pm
Royal Free Hampstead NHS Trust
344 - 354 Gray's Inn Road
London
WC1X 8BP

Action Points

1. Dr Mackie to bring the completed evaluation of newborn screening for Maple Syrup Urine Disease (MSUD), Homocystinuria (pyridoxine unresponsive), Glutaric Aciduria Type I (GA1), Isovaleric Acidaemia (IVA) and Long-chain 3 - hydroxyacyl CoA dehydrogenase deficiency (LCHADD*)* to a future UK NSC meeting.

2. Dr Mackie to bring the pulse oximetry screening for CCHD review to the next meeting.

3. Dr Mackie to write to the National Centre for Human Retrovirology regarding approaching specialised commissioners about HTLV-1.

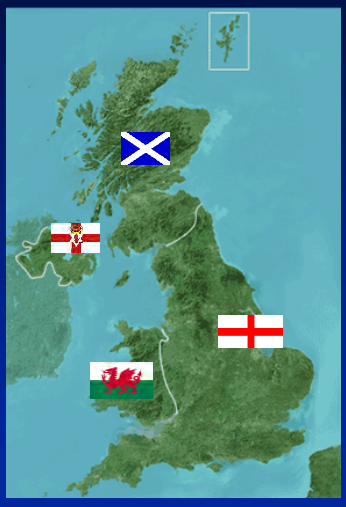
4. Mr Nick Waddell to produce Q&A on GBS and publish it on the UK NSC website.

5. Dr Mackie to contact stakeholders about the GBS action points.

6. Dr Mackie to bring ScHARR's revised prostate cancer screening model to the next UK NSC meeting.

7. The Scottish Government to bring the results of the RCT on FS to a future UK NSC meeting.

Guaiac FOBT Screening

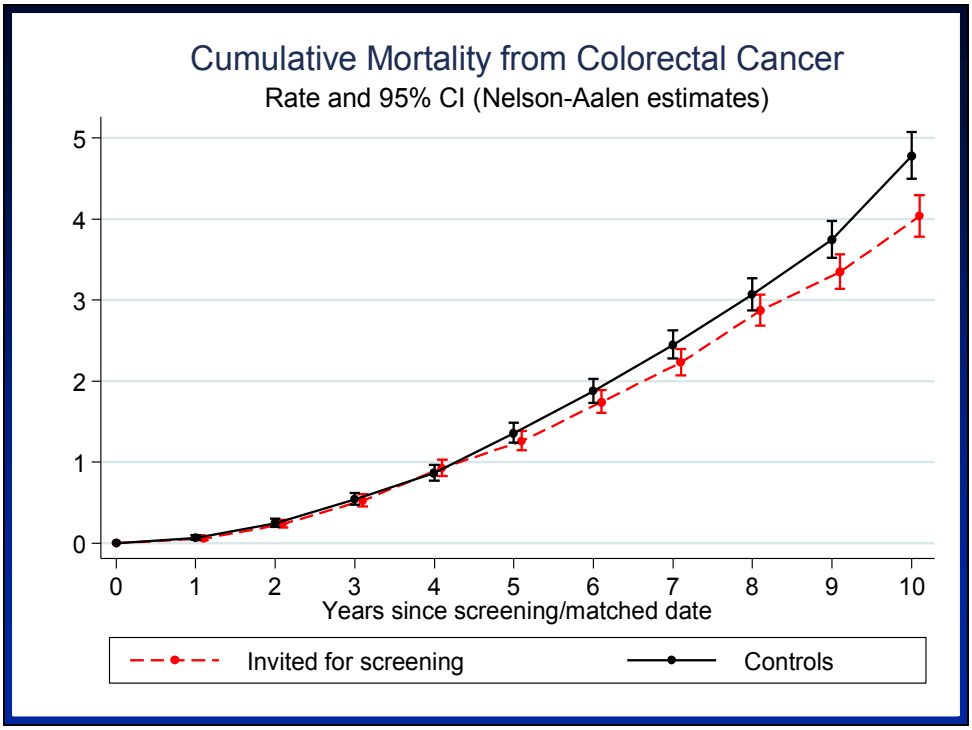


Organisation of the bowel cancer screening programme - Scotland

Single Centre

Investigation and treatment devolved to health boards (n=14)

Age range 50 - 74



Rate ratio of Colorectal Cancer invited vs controls

Overall

0.90 (0.830 – 0.989)

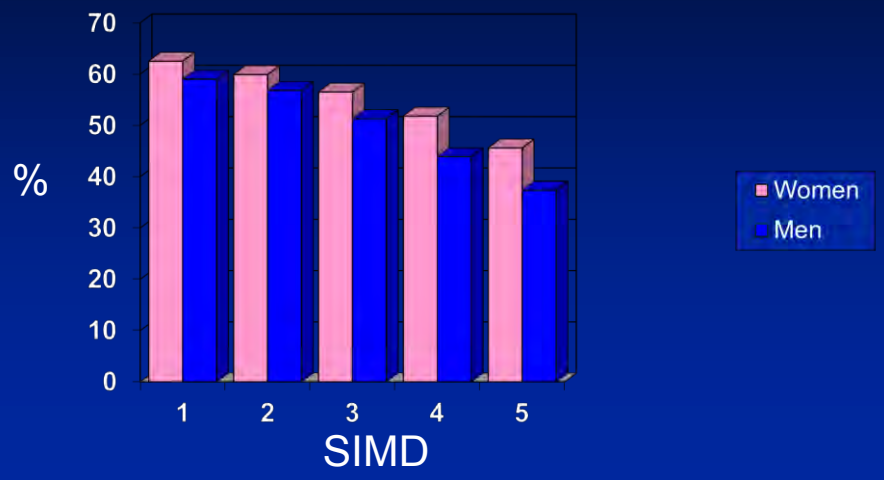
Relative reduction in CRC mortality 10%

Participants only

0.73 (0.653 – 0.824)

Relative reduction in CRC mortality 27%

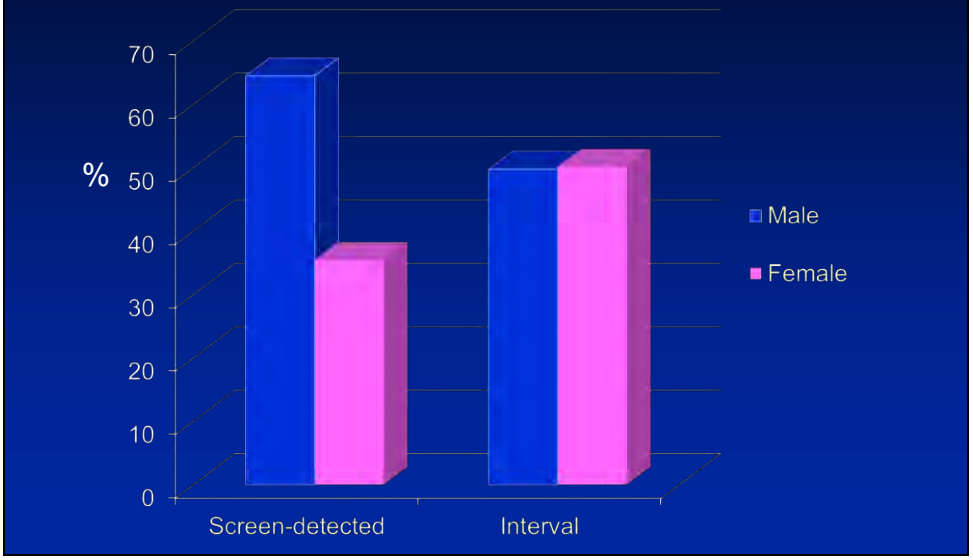
Uptake
- Gender and Deprivation



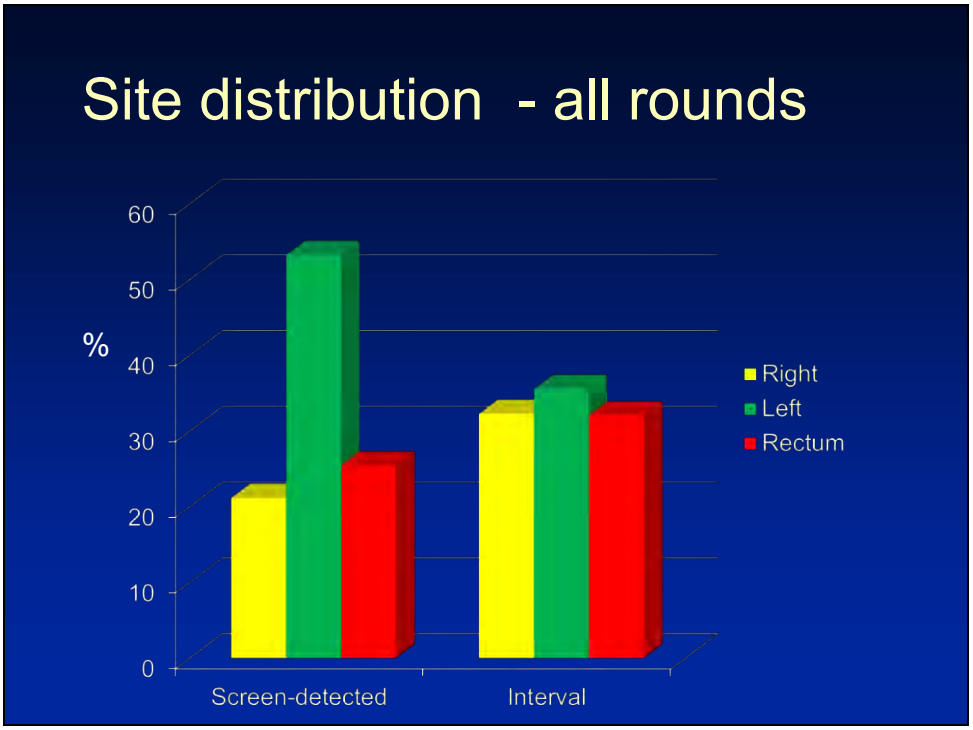
Cancers Diagnosed in the Screened Population

	Round 1	Round 2	Round 3
Screen -detected	351 (56.6%)	208 (46.5%)	139 (35.7%)
True interval	193 (31.2%)	213 (47.7%)	229 (58.9%)
Missed	2 (0.3%)	4 (0.9%)	2 (0.5%)
Miscellaneous	66 (10.7%)	22 (4.9%)	19 (4.9%)
Not on Socrates	6 (1%)	0	0

Gender distribution - all rounds



Site distribution - all rounds



Issues to address

- Uptake
- Interval Cancers
  - Gender inequality
  - Rectal and right-sided cancers

Uptake

- "User-friendly" tests
- "Teaser" letters
- Psychological interventions
- Early contact with health professional
- Better information
- GP involvement
- Publicity campaigns

Interval Cancers

- Increase sensitivity of FOBT
  - Quantitative FIT
- Endoscopic screening
- Novel screening markers

ICRF/MRC Study

(Oct 1996 – March 1999)

- Single flexible sigmoidoscopy *with removal of adenomas*
  - 55-64 years
- High risk ⇒ colonoscopy
  - adenoma > 1cm
  - 3+ adenomas
  - tubulovillous or villous histology
  - 20+ hyperplastic polyps above distal rectum
  - cancer

ICRF/MRC Study

Total no: 354262

↓

Interested : 194726 (55%)

↓

Randomised: 170432

↓ ↓

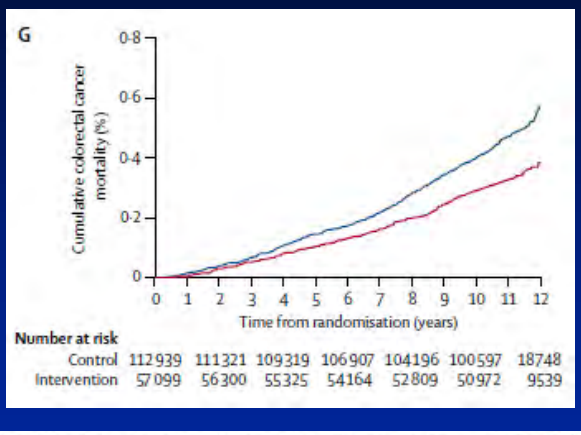
Control: 113178

Invited for screening: 57254

↓

Attended: 40674 (71%)

Mortality from CRC

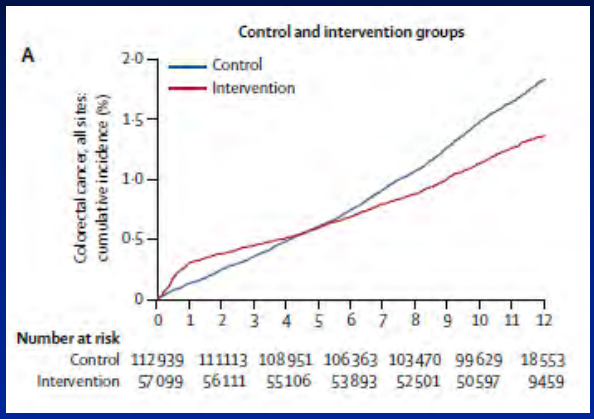


Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

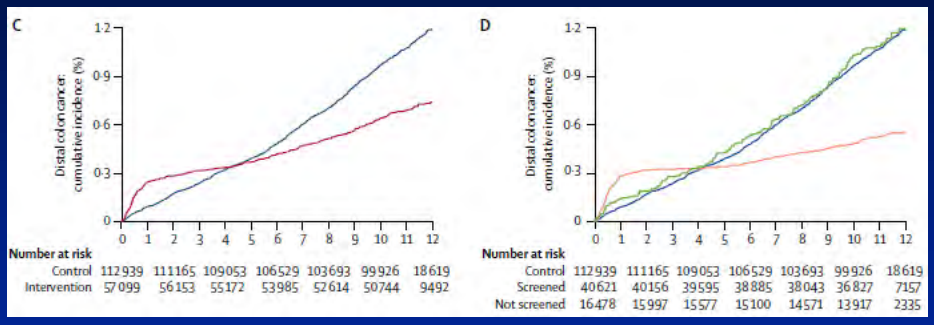
Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

Published Online April 28, 2010
DOI:10.1016/S0140-6736(10)60551-X

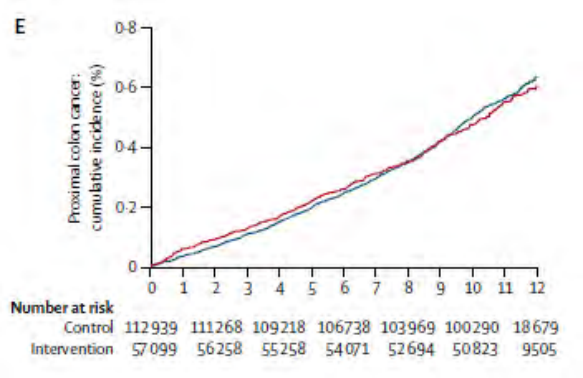
Incidence of CRC



Incidence of *L-sided* CRC



Incidence of *R-sided* CRC



Potential Advantages of FS

- Disease prevention
  - Enhanced detection of left-sided adenomas
- Detection of rectal cancer
- Unlikely to be a gender difference

Potential Problems with FS

- Uptake
  - May be <30% (FS Study, Pathfinders)
  - Possibility of exaggerated deprivation gradient
- Effect on right-sided cancers

Combination of FS and FOBT?

- FS
  - Enhanced screening for rectum and L colon
  - Prevention
- FOBT
  - “Safety net” for those who choose not to undergo FS
  - Detection of R-sided cancers

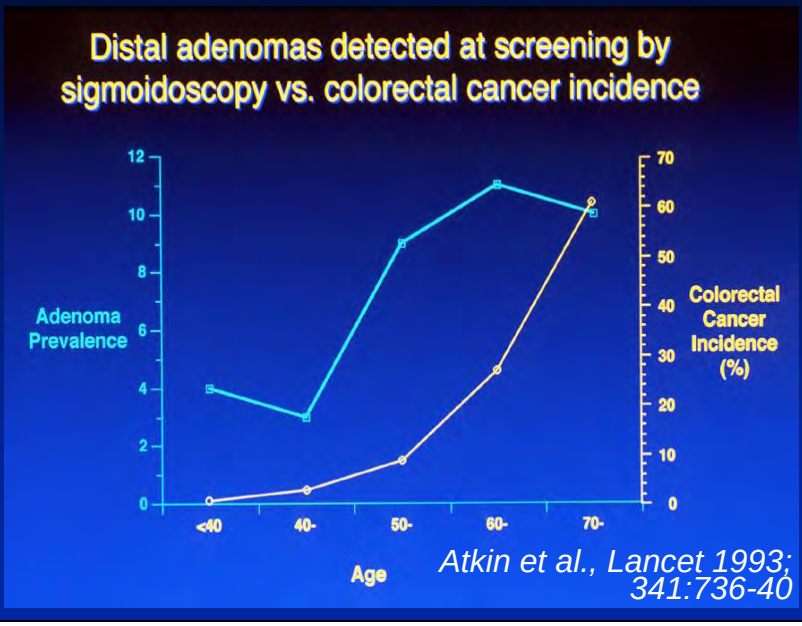
Future of FS in Scotland?

- Commitment to role out in England
  - At age 55 before FOBT screening starts
- Position in Scotland
  - FOBT screening starts at age 50
  - What is added value of FS in a population that has been offered FOBT?

Questions

- Is FS screening feasible in Scotland?
- What is the uptake in an unselected Scottish population?
- What is the effect of gender and deprivation on uptake?
- What is the effect of offering FS on the overall uptake of screening?
- What is the added benefit in FOBT screened population?

What is the ideal age for FS?



Atkin et al., Lancet 1993; 341:736-40

Proposal

- £2 m available
- Evaluation of FS offered at around the age of 60 *in addition* to current FOBT programme
- Greater Glasgow
  - Urban environment
  - High levels of deprivation
- Tayside
  - Mixed urban/rural environment
  - Well established FOBT screening

Issues

- Invitation system
- Information
- Delivery of bowel prep
- Provision of FS
- QA of FS
- Data capture and analysis

Numbers and Costs

- 8,000 FS - £1.6m
- 800 Colonoscopies - £200,000
- Pathology - £80,000
- Total £1.88m

Evaluation or RCT?

- Evaluation
  - Proven screening technology
  - Fewer ethical issues
- RCT
  - Easier to estimate effect of adding FS

Comparison of screening from age 20 and age 25

Table of harms and benefits

- The following table shows what would happen between ages 20 and 26 (inclusive) in terms of number of screens, women with abnormal test results, referrals to colposcopy and women treated per 100,000 women screened from age 20 compared to screening from age 25. It also includes estimates of the numbers of cancers (aged 20-29) in the two groups. We use published screening data from England and from Wales as well as cohort data from the NHSCSP audit of invasive cervical cancer.
- In the table the number of screening episodes and the number of non-negative test results are rounded to the nearest thousand. The number of referrals to colposcopy and the number of women treated are rounded to the nearest hundred.
- The figures are linked to explanations justifying each number.

Note: In the explanations of the figures we use rounded percentages. However, if we would have used the unrounded one, the resulting numbers are only slightly different so that the table of harms and benefits, which includes the rounded numbers to the nearest thousand or hundred, would be the same.

	Age group	100,000 women screened from age 20	100,000 women screened from age 25	Difference
Screened	20-24	124,000	0	
	25-26	51,000	55,000	
	Sum	175,000	55,000	**120,000**
Non-negative test results	20-24	26,000	0	
	25-26	7,000	9,000	
	Sum	34,000	9,000	**25,000**
Referred to colposcopy	20-24	10,500	0	
	25-26	3,400	4,500	
	Sum	13,900	4,500	**9,400**
Treated (Excision, Ablation)	20-24	4,400	0	
	25-26	1,800	2,500	
	Sum	6,200	2,500	**3,700**
Cancers (stage 1A)	20-24	9	0	
	25-29	30	35	
	Sum	39	35	**4**
Cancers (stage 1B+)	20-24	11	13	
	25-29	45	47	
	Sum	56	60	**-4**
Cancers (All)	20-24	20	13	
	25-29	75	82	
	Sum	95	95	**0**

Number of screening episodes between ages 20 and 24 assuming 100,000 women are invited three-yearly from age 20

- 124,000 is based on the number of women aged 20-24 screened in the financial year 2010/11 in Wales. In that year 26,836 [Table 8a, Wales 2010-11*] women had at least one adequate screening test out of a population of 107,870 [Table 1, Wales 2010-11*]. Multiplying by five, we estimate the number of screening episodes to be **124,390**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

Number of screening episodes between ages 25 and 26 assuming 100,000 women are invited three-yearly from age 20

- 51,000 is based on the number of women aged 25-29 screened in the financial year 2010/11 in Wales. In that year 25,104 [Table 8a, Wales 2010-11*] women had at least one adequate screening test out of a population of 98,908 [Table 1, Wales 2010-11*]. Multiplying by two, we estimate the number of screening episodes to be **50,762**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

Number of screening episodes between ages 20 and 24 assuming 100,000 women are invited three-yearly from age 25

- This number is assumed to be **zero** because even if some women are screened from age 20, this by definition will be outside of the screening programme.

Number of screening episodes between ages 25 and 26 assuming 100,000 women are invited three-yearly from age 25

- 55,000 is based on the number of women aged 25-29 screened in the financial year 2010/11 in England. In that year 543,316 [Table 8, England 2010-11**] women had at least one adequate screening test out of a population of 1,976,700 [Table 2, England 2010-11**]. Multiplying by two, we estimate the number of screening episodes to be **54,972**.
- There is little data on whether the numbers screened aged 25-29 would be affected by the age of first invitation. Since the numbers screened per 100,000 are slightly higher in England than Wales, we use the figure for England here because (i) screening does now start from age 25 in England and (ii) these data result in a smaller difference in the total numbers of screening episodes from age 20 to 26 using the two strategies.

** Cervical Screening Programme – England, 2010-11: Report is available on http://www.ic.nhs.uk/

Number of non-negative test results between ages 20 and 24 assuming 100,000 women are invited three-yearly from age 20

- The number of non-negative tests results is obtained by multiplying the number of screening episodes by the proportion of women with a non-negative (borderline changes or worse) test in the year.
- Based on data for women aged 20-24 in Wales in 2010/11, 21.1% (5,662) of those (26,836) with an adequate test had a non-negative result [Table 8a, Wales 2010-11*].
- Multiplying the number of screening episodes between ages 20 and 24 (124,390) by 21.1%, we estimate the number of non-negative test results to be **26,246**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

Number of non-negative test results between ages 25 and 26 assuming 100,000 women are invited three-yearly from age 20

- The number of non-negative tests results is obtained by multiplying the number of screening episodes by the proportion of women with a non-negative (borderline changes or worse) test in the year.
- Based on data for women aged 25-29 in Wales in 2010/11, 14.5% (3,631) of those (25,104) with an adequate test had a non-negative result [Table 8a, Wales 2010-11*].
- Multiplying the number of screening episodes between ages 25 and 26 (50,762) by 14.5%, we estimate the number of non-negative test results to be **7360**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

Number of non-negative test results between ages 25 and 26 assuming 100,000 women are invited three-yearly from age 25

- The number of non-negative tests results is obtained by multiplying the number of screening episodes by the proportion of women with a non-negative (borderline changes or worse) test in the year.
- Among the controls in the national audit of cervical screening [Audit England 2011[#]], it is observed that the proportion of screening tests that are borderline or mild is about 10% greater among women not screened in the previous 3-5 years compared to among women screened 3-5 years earlier. Similarly the proportion of moderate or worse cytology was about 35% greater (for details see here).
- Based on data for women aged 25-29 in England in 2010/11, 13.1% (71,022) of those (543,316) with an adequate test had a non-negative result [Table 8, England 2010-11[**]]. Since the proportion of non-negative tests is less in England than in Wales, we use instead, the proportion from Wales in order to minimise our estimate of the difference in the number of non-negative tests between the two scenarios.
- In Wales the proportion of borderline and mild test in women aged 25-29 was 11.2% (2,812 of those 25,104 with an adequate test result [Table 8a, Wales 2010-11[*]]) and the proportion of moderate or worse was 3.3% (819 of those 25,104 with an adequate test result [Table 8a, Wales 2010-11[*]]).
- The proportion of non-negative tests aged 25-26 in women not screened previously is thus estimated as 11.2%*1.1+3.3%*1.35= 16.8%.
- Applying this to the number of women screened aged 25-26, yields **9,235** women with a non-negative test.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

** Cervical Screening Programme – England, 2010-11: Report is available on http://www.ic.nhs.uk/

NHSCSP audit of invasive cervical cancer, National Report 2007-2010, published July 2011: Report is available on http://www.cancerscreening.nhs.uk/

Relative risk of abnormal test result at age 25-26 in those first screened at 25-26 compared to those also screened aged 20-24

- The analysis is based on population controls born on or after 1 January 1968.
- There were 1189 control women with an adequate cytology result at age 25 or 26 (actually aged between 24.67 and 27.33) who did not have a cytology test between aged 20-24 (actually 19.67-24.67 nor within 5.5 years of their first test after age 24.67). The results of their first such test are recorded in the table.
- The first adequate result after a gap of at least 2.5 years for 2902 women aged 25-26 years, who also had an adequate cytology result aged 20-24 (actually between 19.67 and 24.67) is tabulated too.
- The group not screened aged 20-24, had a relative risk of low-grade cytology at age 25-26 of 1.09 (95% CI: 0.87 to 1.37) compared to those screened age 20-24. Similarly for a high-grade cytology result the relative risk was 1.34 (0.88 to 2.04). Adjustment for region of the country and/or calendar year of the test made little difference. For convenience we round the relative risks to 1.10 and 1.35 respectively.

	Not screened 20-24	Screened 20-24	Relative Risk	95% CI
Normal	1055	2616		
Low-grade	101 (8.5%)	226 (7.8%)	1.09	(0.87-1.37)
High grade	33 (2.8%)	60 (2.1%)	1.34	(0.88-2.04)
Total	1189	2902		

Number of referrals to colposcopy between ages 20 and 24 assuming 100,000 women are invited three-yearly from age 20

- The numbers referred to colposcopy are estimated assuming that all women with moderate or worse dyskaryosis and that 30.8% of women with borderline or mild dyskaryosis are referred.
- The figure 30.8% is based on an average of data from Wales and England (for details see here).
- Based on data for women aged 20-24 in Wales in 2010/11, 18.3% (4,904) of those (26,836) with an adequate test had a borderline or mild result and 2.8% (758) of those (26,836) with an adequate test had a moderate or worse result [Table 8a, Wales 2010-11*]. Thus, we estimate the number of moderate and worse to be 2.8%*124,390 = 3,483 and the number of borderline and mild to be 18.3%*124,390 = 22,763. Of the latter, 30.8% = 7,011 will be referred, yielding a total number referred of **10,494**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

Number of referrals to colposcopy between ages 25 and 26 assuming 100,000 women are invited three-yearly from age 20

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- Based on data for women aged 25-29 in Wales in 2010/11, 11.2% (2,812) of those (25,104) with an adequate test had a borderline or mild result and 3.3% (819) of those (25,104) with an adequate test had a moderate or worse result [Table 8a, Wales 2010-11*]. Thus, we estimate the number of moderate and worse to be 3.3%*50,762 = 1,675 and the number of borderline and mild to be 11.2%*50,762 = 5,685. Of the latter, 30.8% = 1,751 will be referred, yielding a total number referred of **3,426**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/

Number of referrals to colposcopy between ages 25 and 26 assuming 100,000 women are invited three-yearly from age 25

- The numbers referred to colposcopy are estimated assuming that all women with moderate or worse dyskaryosis and that 30.8% of women with borderline or mild dyskaryosis are referred.
- The figure 30.8% is based on an average of data from Wales and England (for details see here).
- Based on earlier assumptions (see here), the number of moderate and worse was 3.3%*1.35*54,972 = 2,449 and the number of borderline and mild was 11.2%*1.1*54,972 = 6,773. Of the latter, 30.8% = 2,086 will be referred, yielding a total number referred of **4,535**.

Referral proportion of women with a borderline or mild test result

- In Wales there were 7,454 women referred to colposcopy considering only the women with referral indication borderline, mild, moderate or worse [Table 16a, Wales 2010-11*] and 3,161 who had a moderate or worse result based on the most significant test result [Table 8a, Wales 2010-11*]. By subtraction there were 4,293 referrals following a lesser abnormality. In total there were 15,292 women whose most significant test result was borderline or mild [Table 8a, Wales 2010-11*]. Thus, the referral proportion is 28.07%. Including the group of women who had a referral due to an inadequate or negative test result, there were 7671 women referred to colposcopy [Table 16a, Wales 2010-11*] and therefore, 4,510 (=7,671-3,161) referrals due to lesser abnormality. For this scenario the proportion of referrals is 29.49%.
- In England there were 105,236 women referred to colposcopy considering only the women with referral indication borderline, mild, moderate and worse [Table 20, England 2010-11**] and 42,076 who had a moderate or worse result based on the most significant test result [Table 8, England 2010-11**]. By subtraction there were 63,160 referrals following a lesser abnormality. In total there were 188,126 women whose most significant test result was borderline or mild [Table 8, England 2010-11**]. Thus, the referral proportion is 33.57%. Including the group of women who had a referral due to an inadequate result (referrals due to a negative test result were not considered in England), there were 107,381 women referred to colposcopy [Table 20, England 2010-11**] and therefore, 63,305 (=107,381-42,076) referrals due to lesser abnormality. For this scenario the proportion of referrals is 33.65%.
- The women who are referred due to an inadequate or negative test result are considered as a special group. Women are only referred after three inadequate test results and women with a negative result are referred for other clinical reasons. Since we base the table on the most significant result in year, where the tests classified as inadequate were excluded, we take the average of the referral proportions from Wales and England excluding the women who had a referral due to an inadequate or negative test result. This leads to a referral proportion of women with a borderline or mild result of **30.8%** (= (28.07%+33.57%)/2). However, including these women the proportions are only slightly different because the amount of women referred to colposcopy due to an inadequate or negative results is very low (0.64% due to an inadequate and 2.2% due to a negative result in Wales [Table 16a, Wales 2010-11*] and 1.5% due to an inadequate result in England [Table 20, England 2010-11**]). Since there are no data by age, we assume that the referral proportion is the same at all ages.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/
** Cervical Screening Programme – England, 2010-11: Report is available on http://www.ic.nhs.uk/

Number of women treated between ages 20 and 24 assuming 100,000 women are invited three-yearly from age 20

- There is not good data on the numbers of women treated. We assume that the number treated is the same as the number with CIN2 or worse on histology. Since there are no data on histology outcome by age, we assume that the positive predictive value of cytology for CIN2+ is the same at all ages.
- In Wales 85.5% of women with moderate or worse dyskaryosis have CIN2 or worse on histology [Table 14d, Wales 2010-11*]. In England the figure is 83.0% [Table 18, England 2010-11**]. We use 84% in these calculations, which is an average of the proportions in Wales and England.
- In Wales 24.9% of women referred with less than moderate dyskaryosis have CIN2 or worse on histology [Table 14b, Wales 2010-11*]. In England the figure is 17.4% [Table 18, England 2010-11**]. We use 21% in these calculations, which is an average of the proportions in Wales and England.
- Based on data for women aged 20-24 in Wales in 2010/11, 18.3% (4,904) of those (26,836) with an adequate test had a borderline or mild result and 2.8% (758) of those (26,836) with an adequate test had a moderate or worse result [Table 8a, Wales 2010-11*]. Thus, we estimate the number of moderate and worse to be 2.8%*124,390 = 3,483 and of the latter, 84% = 2,926 will be treated. The number of referrals due to a borderline and mild test result is 30.8%*18.3%*124,390 = 7,011. Of the latter, 21% = 1,472 will be treated, yielding a total number treated of **4,398**.
- There are also data on the rates of CIN3 registered in women aged 20-24. In Scotland, the rates in 2008 were 359 per 100,000 (461 aged 25-29). Over 5-years this would yield 1,795 per 100,000. If only 50% of treated women have CIN3 (with the rest having CIN2 or less), then it is reasonable to estimate the number treated to be around 3500. This is slightly lower than the figure we use, but it is based on data from Scotland due to a lack of data from Wales.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/
** Cervical Screening Programme – England, 2010-11: Report is available on http://www.ic.nhs.uk/

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** Cervical Screening Programme – England, 2010-11: Report is available on http://www.ic.nhs.uk/

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- Based on earlier assumptions (see here), the number of moderate and worse was 3.3%*1.35*54,972 = 2,449 and of the latter, 84% = 2,057 will be treated. The number of referrals due to a borderline and mild test result is 30.8%*11.2%*1.1*54,972 = 2,086. Of the latter, 21% = 438 will be treated, yielding a total number treated of **2,495**.

* Cervical Screening Programme – Wales, 2010-11: Report is available on http://www.screeningservices.org.uk/
** Cervical Screening Programme – England, 2010-11: Report is available on http://www.ic.nhs.uk/

Number of stage 1A and stage 1B+ cancers in women aged 20-24 with screening from age 20

- The number of stage 1A cancers in women aged 20-24 with screening from aged 20 is based on the proportion of cancers in women aged under 25 in the cervical screening audit that were stage 1A. In Wales of 40 cancers in women aged under 25, 35 had stage recorded in the audit and 40% of these were stage 1A [Table 7 and Table 7a, Audit Wales 2012[##]]. In England, 48% of cancers in this age-group with stage recorded were stage 1A [Table 6a, Audit England 2011[#]]. The average rate of cervical cancer in women aged 20-24 in Wales between 2004 and 2009 was 4.1 per 100,000 (see table below). This rate is slightly lower than in Scotland (4.4), but considerably higher than in England (3.0). Between 1995 and 2004, the rates per 100,000 in Wales and England were 2.4 and 2.5, respectively. In Wales the rates are particularly high since 2005, whereas in England the rates have never been that high. We use a rate of 4/100,000, which is at the high end of what has been observed in the UK, yielding 20 cancers per 100,000 women over 5 years. Assuming 45% are stage 1A yields **9** stage 1A and **11** stage 1B+ cancers.

Mean rates (per 100,000) of cervical cancer in women aged 20-24

Country	1985-89	1990-94	1995-99	2000-04	2005-09
England	2.2	2.2	2	3	2.9
Scotland	2.6	2.3	2.9	4.6	4.1
Wales	4.4	1.8	2.4	2.3	5.9

[#] NHSCSP audit of invasive cervical cancer, National Report 2007-2010, published July 2011: Report is available on http://www.cancerscreening.nhs.uk/

[##] Cervical Screening Wales Audit of Cervical Cancer (CSWACC), National Report 1999-2009, in press

Number of stage 1A and stage 1B+ cancers in women aged 25-29 with screening from age 20

- The number of stage 1A cancers in women aged 25-29 with screening from aged 20 is based on the proportion of cancers in women aged 25-49 in the cervical screening audit that were stage 1A. In Wales of 32% of cancers in women aged 25-49 with stage recorded were stage 1A [Table 7a, Audit Wales 2012[##]]. The corresponding figure in England was 49% [Table 6a, Audit England 2011[#]]. Taking into account that 40% of cancers in women aged under 25 in Wales were 1A, we use 40% for the proportion in women aged 25-29. The average rate of cervical cancer in women aged 25-29 in Wales between 2000 and 2009 was 15.8 per 100,000. This rate is slightly higher than in Scotland (15.0), but considerably higher than in England (12.4). Between 1995 and 2004, the rates per 100,000 in Wales and England were 11.0 and 9.7, respectively. We use a rate of 15/100,000 yielding 75 cancers per 100,000 women over 5 years. Assuming 40% are stage 1A yields **30** stage 1A and **45** stage 1B+ cancers.

Mean rates (per 100,000) of cervical cancer in women aged 25-29

Country	1985-89	1990-94	1995-99	2000-04	2005-09
England	11.1	9.1	9.8	9.6	15.2
Scotland	11.4	12.4	13	13.6	16.3
Wales	12.6	9.5	10.3	11.7	19.8

[#] NHSCSP audit of invasive cervical cancer, National Report 2007-2010, published July 2011: Report is available on http://www.cancerscreening.nhs.uk/

[##] Cervical Screening Wales Audit of Cervical Cancer (CSWACC), National Report 1999-2009, in press

Number of stage 1A cancers in women aged 20-24 with screening from age 25

- The number of stage 1A cancers in women aged 20-24 with screening from aged 25 is put to **zero**, because we assume that stage 1A cervical cancer is asymptomatic and in the absence of screening all cancers would be diagnosed at stage 1B or worse. In practice there would be a small proportion of stage 1A cancers diagnosed incidentally to symptoms from some other pathology.

Number of stage 1A cancers in women aged 25-29 with screening from age 25

- The number of stage 1A cancers in women aged 25-29 with screening from age 25 is based on the number of stage 1A cancers in this age group in those screened from age 20 (n=30) plus the number of stage 1A cancers normally diagnosed aged 20-24 that have not yet been diagnosed as stage 1B+ cancer (n=7). These numbers must be modified by the number of the 7 stage 1A cancers that will have progressed to stage 1B+ without being symptomatically detected by age 25 (assumed here to be 2). Thus, we estimate the number of stage 1A cancers to be **35**. We should also take into account that some screen-detected stage 1B+ cancers at age 26 would be screen-detected stage 1A at age 25. The steeply increasing incidence with age means that this beneficial effect of screening from age 25 may counterbalance any progression of cancers that might have been screen-detected at age 23. Nevertheless we conservatively assume there to be no cancers down-staged as a result of screening at age 25 compared to screening at age 23 and again at age 26.
- Additionally and possibly more controversially, we assume that none of the CIN3 that might have been treated aged 20-24 would have progressed to cancer by age 25. This is supported by observations regarding the rates of CIN3 registrations compared to the rates of cervical cancer incidence [1] and by the lack of association between screening in women aged 20-24 and subsequent cancer incidence [2].

1. Sasieni P, Castanon A, Parkin DM. How many cervical cancers are prevented by treatment of screen-detected disease in young women? *Int J Cancer*. 2009 Jan 15;**124**(2):461-4
2. Sasieni P, Castanon A, Cuzick J. Effectiveness of cervical screening with age: population based case-control study of prospectively recorded data. BMJ. 2009 Jul 28;339:b2968. doi: 10.1136/bmj.b2968. Erratum in: BMJ. 2009;339:b3115

Number of stage 1B+ cancers in women aged 20-24 with screening from age 25

- The number of stage 1B or worse cancers in women aged 20-24 with screening from age 25 is put to **13** consisting of the 11 such cancers that occur with screening from age 20 and 2 more due to progression of 2 of the 9 asymptomatic stage 1A cancers to symptomatic stage 1B+ cancer by the age of 25. This number is somewhat arbitrary but is supported by the observation that neither the number of all cancers nor the number of stage 1B or worse cancers in women aged 20-24 was seen to be reduced by screening from age 20 [Sasieni et al 2009]. Thus, we allow for a modest (~20%) increase in stage 1B+ cancers in women aged 20-24 and an overall decrease in cervical cancer in this age group in the absence of screening.

Sasieni P, Castanon A, Cuzick J. Effectiveness of cervical screening with age: population based case-control study of prospectively recorded data. BMJ. 2009 Jul 28;339:b2968. doi: 10.1136/bmj.b2968. Erratum in: BMJ. 2009;339:b3115

Number of stage 1B+ cancers in women aged 25-29 with screening from age 25

- The number of stage 1B or worse cancers in women aged 25-29 with screening from age 25 is calculated under the assumption that the overall number of cancers aged 20-29 is not affected by screening from age 20 compared to age 25. Thus, the total number of cancers is 95 and with 35 stage 1A cancers there must be 60 stage 1B or worse. Since 13 of these were diagnosed aged 20-24 there must be **47** at age 25-29.