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Editorial Comment

Cervical cancer screening in Europe – Changes over the last 9 years

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The first studies showing a large impact of high-quality cervical cancer screening activity were published in the 1960s and 1970s and documented a decrease in the incidence of invasive squamous-cell carcinoma of the cervix uteri among women screened of up to about 90%, in comparison with those unscreened or the rates before screening.¹ It has been estimated that high quality screening can reduce cervical cancer incidence by 80% or possibly more in the whole screened population.² This large reduction, the relatively early age of occurrence of cervical cancer and the fact that cervical cancer screening prevents invasive cancer (with obvious impact on quality of life) give it high priority despite the fact that cervical cancer incidence, even before the advent of screening, was lower than that of other cancers subject for screening.

The first cervical cancer screening programmes in Europe were initiated in the 1950s and early 1960s. In the following years organised population-based programmes, or spontaneous (opportunistic) screening activities based on the Papanicolaou smear test, have developed in almost every European Union member country. In 2000, a first special issue of the *European Journal of Cancer* described the situation of cervical cancer screening in the European Union.³

Over the last years, cervical screening has been a field in rapid evolution and a further acceleration of these changes can be expected in the next few years. Knowledge on the

role of Human Papillomavirus (HPV) as the causative agent of cervical cancer has resulted, on one hand, in the availability of prophylactic vaccines with high efficacy in reducing vaccine-type HPV infections and high-grade pre-cancerous lesions (reviewed in 4). On the other hand, new screening techniques, particularly those based on HPV detection, have been proposed and evaluated using severe pre-cancerous lesions as the outcome. The European contribution in this field has been relevant: randomised trials conducted in Sweden,⁵ the Netherlands,⁶ England,⁷ Italy⁸ and Finland⁹ have concluded or are close to conclusion. Also, during these years, the European Union has expanded with the inclusion of countries from Eastern Europe. These countries share problems, different from those of the old members states, related to a different history of cervical screening, higher incidence and mortality from cervical cancer – frequently with increasing trends – and lower available resources. This special issue of the *European Journal of Cancer* aims at updating the situation in this new overall scenario.

The first two papers, reporting the available information on HPV infection¹⁰ and on trends of cervical cancer mortality,¹¹ together with recently published data on cervical cancer incidence,^{12,13} provide the background epidemiological information on the burden of cervical cancer and on its main risk factor. Unfortunately, lack of historical data on HPV prevalence

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limits the possibility of using such data to interpret mortality and incidence trends. The latter, however, provide elements for an evaluation of the historical impact of cervical screening practice.

High population coverage and high quality of the screening process are essential to achieve high effectiveness of screening at a population level. In addition, high screening quality is essential to avoid the potential side-effects of cervical screening. The European Union issued recommendations on cancer screening suggesting population-based organised programmes¹⁴ and published related quality-assurance guidelines for cervix cancer screening.¹⁵ Despite the long-lasting activities in most EU member countries, there are still few earlier reports monitoring these programmes and practically none comparing European countries regarding process performances of screening. This special issue includes summary data on the current cervical screening policies¹⁶ and on monitoring and performance indicators,¹⁷ based on the screening registers established thus far in the member countries and considering cytological screening, the screening technique currently largely adopted in Europe.

Given the high diversity of the status of cervical screening in European countries, it is, however, difficult to summarise it in a few quantitative parameters and it is important to underline the peculiarities of each country, also in order to allow a correct interpretation of summary results. Therefore, this special issue also presents brief descriptions of the current national situation of cervical cancer screening from all but one of the member states.¹⁸ These papers include updated documentation of the most relevant publications. In addition, two summary papers discuss, separately, data on the challenges of organising cervical screening in the old¹⁹ as well as the new member countries.²⁰

As previously stated, it can be expected that cervical screening will be deeply changed over the next few years by the introduction of HPV vaccination (which several European Union member countries have already started to integrate in their vaccination programmes) and, possibly, by the adoption of new screening techniques. A specific paper reports information about decisions on the HPV vaccination.²¹ This special issue ends with a discussion about the foreseeable future based on currently available data.²²

The articles in this special issue show that the extension of population-based cervical screening programmes in the European Union has increased but still only includes approximately one third of the approximately 140 million women potential target population in the European Union.²³ As a result, screening coverage is still suboptimal despite a very high consumption of screening tests, and also because some countries adopt very intensive screening policies^{16,17} associated with low cost-effectiveness.²⁴ In most member states the overall volume of screening tests is sufficient in order to invite women with 3- or 5-yearly intervals. The systematic registration of data to monitor the screening process has also increased but still includes a limited proportion of the European population¹⁶ so that an evaluation of the quality of screening process is still not possible for the remaining women. Despite problems of comparability, due to different registration and classification systems, we observed a high variability in performance parameters be-

tween European countries.¹⁷ These can only partly be explained by a different baseline risk^{10,18} but seem largely related to differences in screening protocols, in variability of cytology interpretation and in the actual attendance to diagnostic work-up, suggesting important differences in the effectiveness and undesired effects of screening between European countries.

According to most recent estimates there are, every year, approximately 34,300 new incident cases of cervix cancer and 16,300 deaths from the disease in the whole European Union¹² (estimated among women aged 0–74 years); 22,700 incident cases and 9500 deaths in the old and 11,600 incident cases and 6800 deaths in the new member countries, respectively. There are annually almost 60,000 incident cases and 30,000 deaths in the whole of Europe.²⁵ Decreases of mortality were over 50% from 1970–74 to 2000–2004 in all the old EU member countries except Ireland.¹¹ If we assume that screening, from Arbyn and colleagues introduction, caused an approximate 60% average decrease, then possibly approximately 35,000 incident cases and 15,000 deaths are already prevented per year in these countries. However, compared to a potential reduction of over 80% with optimal screening, in most of these countries the current incidence and death rates could, however, still be largely reduced. The potential benefit in relative terms is even larger in the new member countries and in many non-member European countries, in most of which no similar historical decrease in the disease burden has taken place.

The new validated HPV-screening methods have shown clearly lower rates of severe pre-cancerous lesions after screening, compared with those after conventional cytology^{5,6} and the absolute rate of severe lesions after a negative HPV test is almost negligible.²⁶ These findings make it likely that the overall impact against cervical cancers could increase from that of conventional cytology. Also, the screening intervals should become longer with consequences on quality of life and provision of new opportunities to increase coverage. Finally, the variability of screening quality due to subjectivity of cytology interpretation could be reduced. However, no relevant impact at a population level can be obtained in absence of high coverage. In addition, if not properly used, these new methods can add greatly to adverse effects and costs. Therefore, it is essential that they are integrated in organised screening programmes.

In conclusion, actions are needed to improve coverage and quality of cervical screening, through the implementation of well monitored population-based programmes and through the standardisation of registration systems between European countries.

Much of the newly-presented data has been collected in connection with the European Union funded European Network for Information on Cancer (EUNICE), coordinated by the International Agency for Research on Cancer, Lyon. A first report of the status of cancer screening programmes²³ has been published in collaboration, on cervical cancer screening, with the authors of the current special issue.

Conflict of interest statement

None declared.

REFERENCES

1. IARC Working Group on Cervical Cancer Screening and UICC Project Group on the Evaluation of Screening Programmes for Cancer. *Screening for cancer of the uterine cervix*. Lyon: IARC Sci Publ., IARC; 1986. p. 1–315.
2. International Agency for Research on Cancer. *Cervix cancer screening*. IARC handbooks of cancer prevention, vol. 10. Lyon: IARC Press; 2005. p. 1–302.
3. Linos A, Riza E, van Ballegooijen M, editors. Cervical cancer screening in the European Union. *Eur J Cancer* 2000;**36**(17):2175–75 [special issue].
4. Arbyn M, Dillner J. HPV vaccination – an overview. In: Arbyn M, Anttila A, Jordan J, et al., editors. *European guidelines for quality assurance in cervical cancer screening*. European Communities. Luxembourg: Office for Official Publications of the European Union; 2008. p. 267–82.
5. Naucleer P, Ryd W, Törnberg S, et al. Human papillomavirus and Papanicolaou tests to screen for cervical cancer. *N Engl J Med* 2007;**357**(16):1589–97.
6. Bulkman NWJ, Berkhof J, Rozendaal L, et al. Human papillomavirus DNA testing for the detection of cervical intraepithelial neoplasia grade 3 and cancer: 5-year follow-up of a randomised controlled implementation trial. *Lancet* 2007. doi:10.1016/S0140-6736(07)61450-0.
7. Kitchener HC, Almonte M, Wheeler P, et al. HPV testing in routine cervical screening: cross sectional data from the ARTISTIC trial. *Br J Cancer* 2006;**95**(1):56–61 [Epub 2006 January 13].
8. Ronco G, Giorgi-Rossi P, Carozzi F, et al. Results at recruitment from a randomized controlled trial comparing human papillomavirus testing alone to conventional cytology as the primary cervical cancer screening test. *J Natl Cancer Inst* 2008;**100**:492–501.
9. Kotaniemi-Talonen L, Nieminen P, Anttila A, Hakama M. Routine cervical screening with primary HPV testing and cytology triage protocol in a randomised setting. *Br J Cancer* 2005;**93**(8):862–7.
10. De Vuyst H, Clifford G, Li N, Franceschi S. HPV in Europe. *Eur J Cancer* 2009;**45**(15):2632–9 [Special issue].
11. Arbyn M, Raifu AO, Weiderpass E, Bray F, Anttila A. Trends of cervical cancer mortality in the member states of the European Union. *Eur J Cancer* 2009;**45**(15):2640–8 [special issue].
12. Arbyn M, Autier P, Ferlay J. Burden of cervical cancer in the 27 member states of the European Union: estimates for 2004. *Ann Oncol* 2007;**18**:1423–5.
13. Karim-Kos HE, de Vries E, Soerjomataram I, Lemmens V, Siesling S, Coebergh JW. Recent trends of cancer in Europe: a combined approach of incidence, survival and mortality for 17 cancer sites since the 1990s. *Eur J Cancer* 2008;**44**(10):1345–89 [Epub 2008 February 14].
14. European Council. Council recommendation of 2 December 2003 on cancer screening. Official Journal of the European Union 16.12.2003: L327/34–L327/38.
15. Arbyn M, Anttila A, Jordan J, et al. *European guidelines for quality assurance in cervical cancer screening*. European Communities. Luxembourg: Office for Official Publications of the European Union; 2008. p. 1–291.
16. Anttila A, von Karsa L, Aasmaa A, et al. Policies for cervical screening programmes in Europe. *Eur J Cancer* 2009;**45**(15):2649–58 [special issue].
17. Ronco G, van Ballegooijen M, Becker N, et al. Process performance of cervical screening programmes in Europe. *Eur J Cancer* 2009;**45**(15):2659–70 [special issue].
18. Working group on the registration and monitoring of cervical cancer screening programmes in the European Union. Description of the national situation of cervical cancer screening in the member states of the European Union. *Eur J Cancer* 2009;**45**(15):2685–708 [special issue].
19. Arbyn M, Rebolj M, De Kok I, et al. The challenges of organising cervical screening programmes in the 15 old member states of the European Union. *Eur J Cancer* 2009;**45**(15):2671–8 [special issue].
20. Nicula FA, Anttila A, Neamtiu L, et al. Challenges in starting organised screening programmes for cervical cancer in the new member states. *Eur J Cancer* 2009;**45**(15):2679–84 [special issue].
21. Lévy-Bruhl D, King LA, O' Flanagan D, et al and the country specific VENICE gate keepers and contact points. The current state of introduction of HPV vaccination into national immunisation schedules in Europe: results of the VENICE 2008 survey. *Eur J Cancer* 2009;**45**(15):2709–13 [special issue].
22. Lynge E, Anttila A, Arbyn M, Segnan N, Ronco G. What's next? Perspectives and future needs of cervical screening in Europe in the era of molecular testing and vaccination. *Eur J Cancer* 2009;**45**(15):2714–21 [special issue].
23. Von Karsa L, Anttila A, Ronco G, et al. Cancer screening in the European Union. Report on the implementation of the Council Recommendation on cancer screening, 1st report. European Communities, printed in Luxembourg by the services of the European Commission, 2008. p. 1–137.
24. Van Ballegooijen M, van der Akker – van Marle E, Patnick J, et al. Overview of important cervical cancer screening process values in EU-countries, and tentative predictions of the corresponding effectiveness and cost-effectiveness. *Eur J Cancer* 2000;**36**(17):2177–88 [special issue].
25. <<http://www-dep.iarc.fr/Globocan>>; 2002.
26. Dillner J, Rebolj M, Birembaut P, et al. Long term predictive values of cytology and human papillomavirus testing in cervical cancer screening: joint European cohort study. *BMJ* 2008;**377**:a1754. doi:10.1126/bmj.a175.