EJGO European Journal of Gynaecological Oncology

Original Articles

"Gynaecological cancer screening" or "cervical screening?" The case of Hungary

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Summary

In Hungary, "gynaecological cancer screening" by gynaecologists having interest in oncology has had a long history. The screening tool was colposcopy alone embedded in complete gynaecological examination. Later on smear-taking for cytology has been added. This screening protocol has survived until now both in the gynaecological community and public. In the meantime, as it proved its effectiveness, cytological examination has been internationally recommended,\ as sole method of organized cervical screening; in case of non-negative test result, gynaecological examination including colposcopy is justified. Smear-taking can be undertaken by trained paramedical personnel. The authors have made an attempt to argue the use of "cervical screening" instead of "gynaecological cancer screening", which is deeply entrenched into both professional and public consciousness in Hungary.

Key words: Cervical screening; Colposcopy; Cytology; Health visitors.

Introduction

Hungary is carrying a heavy burden of cervical cancer. Regarding mortality, it may be found in the list of mortalities in the last quarter among the European countries (Figure 1). Cervical screening, as a public health policy, has proved its effectiveness in terms of reduction of morbidity, and mortality from the target disease in the target population (Figure 2) [1], and a wide application of morphology-based cervical cytology (Pap smear) as screening tool is strongly recommended by international bodies [2, 3]. Hungary (a Central-Eastern European country, population ten million, one of the "countries in transition" which joined the European Union in 2004), cervical screening had undergone several developmental stages [4].

History of cervical screening on Hungary

In Hungary, the history of opportunistic cervical screening dates back to the late 1950s. At the beginning, the screening tool was *colposcopy alone,* sporadically applied by gynaecologists engaged in practicing oncological gynaecology. In 1954, a ministerial decree was issued, declaring that "mass screening must be conducted in such a way that each woman over 30 years of age be screened by colposcopy" (MOH 8834/31/1954). There are no data on its effect.

In the meantime, *exfoliative cytology* has been extensively investigated, as a method of early detection of potentially pre-cancerous lesions (cervical intraepithelial neoplasia [CIN I-III.]), and early cancer of the uterine cervix, with particular attention to those located in the transformation zone and endocervical canal. Since mid 1960s more and more cytology laboratories – based on pathology departments – had been set up in Hungary. In 1972, a "School of Cytotechnologists" to provide regular training for "pre-screeners" was established, and the system of "pre-screening" introduced. By the end of 1970s, the sufficient capacity to meet the demands of three-yearly cytology screening of entire eligible population was in place [5].

By the end of 1970s, more and more gynaecologists became experienced in the practice of colposcopy. In 1976, a joint deliberation by the Board of Gynaecology and Board of Oncology was issued saying that "every gynaecological examination should be performed as screening", and, "no cervical screening without cytology" [6]. C*olposcopy completed by cytology* had become the screening protocol: the smear-taking by gynaecologists as well as colposcopy had been carried out as part of a complete gynaecological examination. In fact, the gynaecologists have monopolised the cervical screening, and "*gynaecological cancer screening* instead of *"cervical screening"* had been the widely recognised practice in the country.

During the 1980s, a country-wide opportunistic "cervical screening programme" had taken place. The annual number of smears analysed exceeded one million, the clinical stage of the detected cervical cancers had favourably shifted,

Revised manuscript accepted for publication February 2, 2016

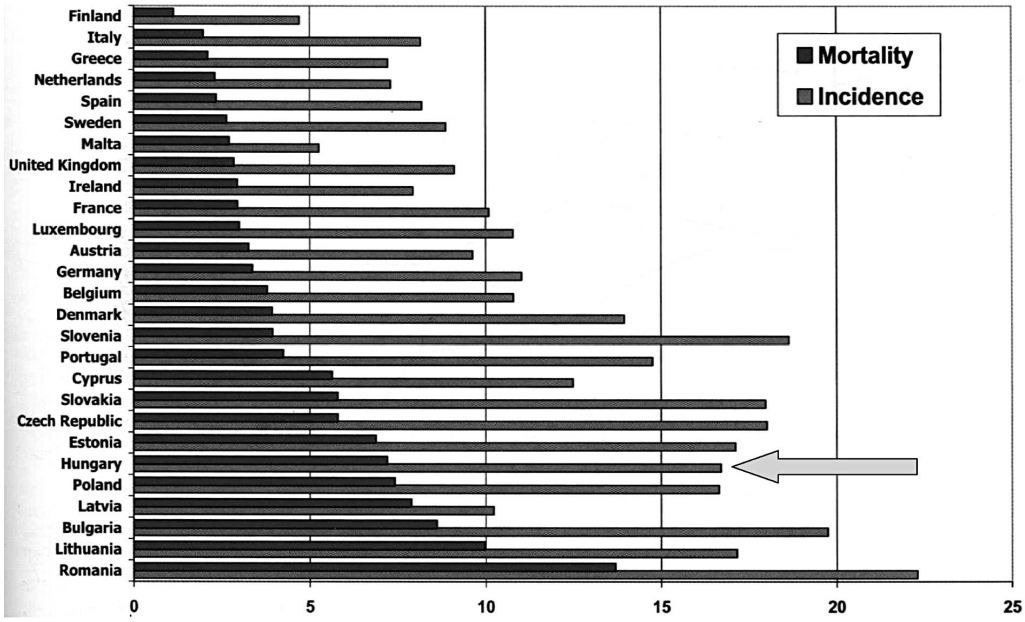

Figure 1. — Cervical cancer: incidence and mortality in the European Countries.

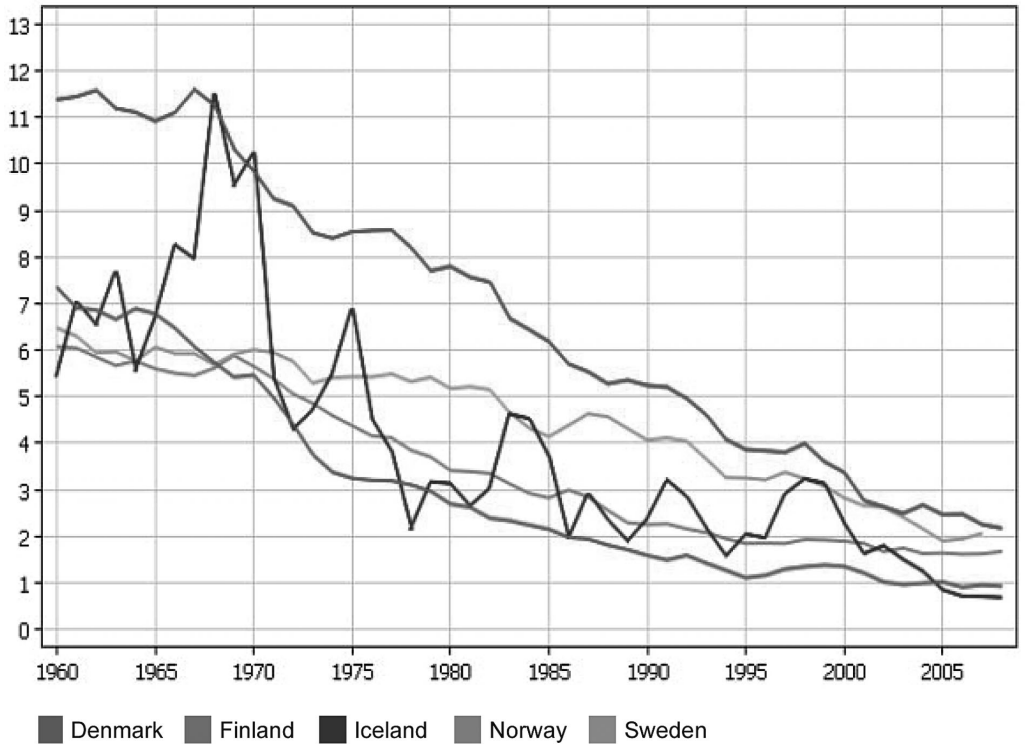

Figure 2. — Mortality from cervical cancer in the Nordic Countries, as function of intensity of screening strategy. Source: Nygård M.: "Screening for cervical cancer: when theory meets reality". *BMC Cancer*. 2011, *11*, 240.

however the mortality rates had not decreased, but did level off at a rather high level (8-10/10^5 population). It has been admitted that the "cervical screening programme" had failed [7]. The reason for failure was obviously the lack of individual identification of women to be screened: only the number of smears analysed was registered, and not the women screened. As a result, certain self-selected women (approximately 30% of the eligible ones) had been screened with unnecessary frequency, while the majority of the women had never been screened.

In the mid 1990s, as part of "secondary prevention of cancer" sub-component of the "Close the gap" programme"

co-sponsored by the World Bank, a "model" cervical screening programme was implemented on a limited scale, with the aim of introducing elements of "organized screening", as recommended by WHO/IARC and UICC [8], and to adopt the recommendation to the local needs and opportunities [9]. The pilot programme has created a favourable policy-environment for integration of organized cervical screening as a core function of the healthcare system.

In 2003, as a component of the National Public Health Programme launched by the Government, a country-wide National Cervical Screening Programme has been established, with the National Chief Medical Officer's Office in charge. All requirements of "supply side" of organised screening have been met [10]. The programme was a nation-wide, provider-initiated, invitation-based organised screening, supported by a National Screening Registry. Its objective was to three-yearly screen the asymptomatic women of 25-64 years of age by cytological analysis of cervical smears, and to refer those with abnormal (*non-negative)* cytology to gynaecological services to further diagnostic procedure including colposcopy and appropriate treatment. Notwithstanding, the gynaecological community has continued the traditional practice and they remained in the driver's seat of cervical screening. Furthermore, they insisted on a bimanual pelvic examination complemented with colposcopy, in addition to smear-taking. All the women eligible for screening received invitation letter, however, the majority of women – without waiting for invitation, or even having received it – have reported themselves for "gynaecological screening" by their "own" (private) gynaecologists, and, these screening examinations had *not* been registered by the National Screening Registry. As a result, the *coverage* of screening (i.e. proportion of women who rejected the invitation and turn up for screening outside the organised programme) has been rather high (approximately 60%), but *compliance* rates (proportion of those women who accepted the invitation, screened inside the programme, and registered by the screening registry have remained unacceptably low (8-10%), and a significant proportion of the female population has never been screened.

The analysis of the reasons for non-attendance at the offered screening showed that one of the main difficulties to overcome is the limited access to the smear-taking gynaecological service, particularly in rural areas where gynaecological services are not available locally. According to the reimbursement data provided by the National Health Insurances Fund, much more smears were taken and analysed outside as compared to inside the programme.

The question presented itself as to whether what is called "population cervical screening" was really a *health policy* and *service-based screening programme*, or a widespread clinical exercise? In the view of gynaecological community (and to certain extent in the conscience of the public at large, too) it seemed to be the latter one. There was an urgent need to reconsider and reorganise the screening practices going by the "state-of-the-art" screening strategy in Hungary, to erase the term of "gynaecological screening" form the consciousness of the women at large.

Efforts to reorganise the screening practices: the role of "health visitors"

2008 was a turning point. The Hungarian National Audit Office carried out an investigation "about the utilisation of the financial resources expended for screening programmes", and as a result they made proposals to the health government to reorganise the cervical screening programmes in line with the international recommendations, practically to apply cytology as *sole screening test,* to bring closer the provision of organised cervical screening to primary care practices; furthermore, the smears be taken by primary care personnel and non-negative cases be referred to gynaecological services for further clarification [10]. Following these recommendations, the health government (Ministry of Human Resources) decided to improve access to screening facilities by intensifying the involvement of primary care personnel, particularly the "health visitors" in the screening process.

Education and training of the health visitors

The *"health visitors"* are the public health nurses, who are ubiquitous, and qualified to provide preventive services to the female population in the country. They are professionals receiving higher education, i.e. a four-year course following the secondary high school graduation. Their activities have been organized at the primary care level, working in close cooperation with local primary care physicians. They have personal contact with virtually all invited women, and they seem suitable for taking the cervical smear, and have easy access to those who have difficulties in seeking gynaecological services [11].

Their new task as smear-takers would have remarkable implication for education and training [12]. First of all, proper communication skill is required when counselling, and providing pre-screening information, while answering questions of the women to be screened. Then, they must have some basic knowledge in epidemiology, anatomy, physiology, and pathology of cervical cancer and precursors. They have to be familiar with the theory and strategies of cervical screening, classification of smears, psychological side-effects, and ways to prevent them. They must know the referral routes to the gynaecological services. In addition, they must have skills in asking the women about their general health, provide information, and gain informed consent. Most importantly, they have to be *skilful in taking smears* from the uterine cervix and the endocervical canal, transfer of cellular material onto the glass slide, fixation and label of the sample, and its transportation to cy-

tological laboratory. Having all these in mind, a curriculum had been designed, approved, and accredited by the relevant authority. It consisted of three elements. The first phase includes a 40-hour theoretical course, presenting all the knowledge as set out above; second, a two-day session on communication with the women to be screened; and third, under supervision of a gynaecologist, a period of training in smear-taking, until they achieved the necessary skill. One is pronounced skillful enough if 30 good quality smears are obtained, as judged by a competent cytopathologist. After having completed the course, the candidates take a final examination, and receive "certificate of competency" that authorises them to carry out cervical screening in their localities according to the screening protocol. Pilot programmes of involving the "health visitors" are promising. In the near future, the knowledge and skill required by cervical screening would be included in the curriculum of graduate education and training of the would-be health visitors, and their screening activities extended nation-wide.

Discussion

By definition, *screening* aims to early detect cancer and its precursors by means of regular examination of predominantly asymptomatic individuals of appropriate age without any complains, using evidence-based screening tests. [13]. It has the potential to significantly reduce the burden of target disease in the population, and to detect malignant tumours, as well as precursor lesions *earlier* than it would be the case without screening, and to refer them for appropriate diagnostic procedure and treatment.

According to the valid "state-of-the-art recommendations", *cervical screening* means *"microscopic analysis of the sample obtained by after visualising the cervix, taken from the ectocervix, transformation zone, and endocervix*" [3]. Cervical screening reduces the incidence of cervical cancer and its precursor lesions, and mortality from cervical cancer, and improves quality of life. The degree of reduction of lesions in question seems to be proportional to the intensity of screening strategy, i.e. the age range, frequency, and interval between consecutive screening episodes (Figure 2) [1]. Cytological screening every three to five years can potentially prevent up to four out of five cases of cervical cancer, and can reduce cervical cancer incidence up to 80% at population level [14]. Such benefits can only be achieved if screening is provided in organized, population-based programmes with quality assurance at all levels [15]. Establishment of screening registries, and linkage of individual screening data with cancer registry data, taking into account appropriate data protection standards and methods, are essential tools of monitoring and evaluation.

In Hungary, gynaecologists traditionally have a key role to play in cervical screening process by taking cervical smears themselves, in addition to assessment by colposcopy and bimanual pelvic examination. In the current "gynaecological screening protocol" physical examination of breasts has been added, that is obviously not suitable for detecting "small" lumps in the breasts which is the ultimate aim of breast screening [16], however, it has been admitted by highly competent gynaecologists that the aim of a "gynaecological cancer screening" is nothing but "cervical screening" [17].

In the beginning, the screening test applied was *colposcopy alone.* Since Hinselmann first described the basic colposcopic equipment and its use establishing the foundation for the practice of colposcopy [18], this optical method was becoming widespread throughout the countries, particularly those under German influence, such as Hungary, and since the 1960s it has been widely used oversees, too. Colposcopy is a *diagnostic procedure* to examine an illuminated, magnified view of the cervix. Many premalignant and malignant lesions in this area have discernible characteristics which can be detected through the examination, allowing the colposcopist to visually distinguish normal from abnormal appearing tissue and take directed biopsies for further pathological examination [19-21]. However, when colposcopy is evaluated for primary screening, it has been accompanied by simultaneous cytology. The rationale beyond this combined testing approach is that it decreases false negative and false positive rates associated to cytology alone, and also reduces the need for call-back for repeat cytology, being used as a guide for collection of the cytology specimen [14].

The unbiased assessment of the accuracy of colposcopy requires the independent verification with a gold standard, which usually relies on histology. Without histological confirmation, colposcopically negative cases are very often considered as truly negative, and in case of endocervical location of the squamo-columnar junction, or glandular cervical lesions, colposcopy may be really false negative. The sensitivity of colposcopy directed biopsy for CIN2+ in women with satisfactory colposcopy was 57-81% [22, 23].

Constraints limiting the application of colposcopy to primary screening include its high costs relative to cytology, the availability and accessibility of trained colposcopist having long enough experience to acquire expertise in recognition of specific patterns in the epithelium of surface of cervix, and – last but not least – the lower ability to detect endocervical lesions. The expert colposcopist may be able to predict the histological diagnosis quite accurately, but in general, the coloscopic-histological correlation is only moderate [24].

Colposcopy continues to be used routinely as standard gynaecological *diagnostic* throughout Europe provided the availability of the instruments and trained colposcopists. The most common reason for referral of women for colposcopy is abnormal cervical cytology discovered as a result of cytological screening. It is important that all women with high-grade abnormalities (CINII-III) be referred im-

mediately for diagnostic colposcopy. Colposcopy is widely used as a clinical diagnostic procedure, but definitely *not recommended as a primary screening tool, particularly not as method for population-oriented mass screening.*

The other element of "gynaecological screening" is the *bimanual pelvic examination*, i.e. palpation to assess the position, size, mobility, lumpiness, tenderness of uterus, as well as the annexes. However, the palpation is obviously not sensitive enough to recognise any lesions of endometrial layer of uterine corpus and the ovaries. This procedure might be clinically justified, but does not bring closer at all to the aims of cervical screening, and does not fit in the public health agenda [25].

The current "gynaecological cancer screening" protocol prescribes a complicated multistep diagnostic procedure performed by medical specialist [16]. Conversely, a screening test as a public health procedure, by definition, should be simple, i.e. easy to perform and interpret acceptable, accurate, reliable, sensitive, and specific [13]. It follows that to link a mass screening examination as a public health measure to clinical diagnostic setting, and to a complex clinical examination, is an obvious fallacy and nonsense.

Gynaecologists have an important, nothing to replace with, role in "second step" of screening: to clarify a case with abnormal cytology, women need to be referred to a gynaecologist who can exclude or confirm the suspicion of malignancy suggested by the cytological examination, in other words, he/she establishes the diagnosis. However, "screening" which takes place opportunistically in the gynaecological practice, on the initiative of the individual woman or her doctor, by colposcopy and pelvic examination in clinical settings, should be discouraged. (Of course, this recommendation does not contradict the necessity of the periodical gynaecological check-up which can be reasonably advised to and expected from each health-conscious woman). Bimanual pelvic examination must not be undertaken as a routine part of sample-taking in asymptomatic women. Such "screening practice" results in high coverage in self-selected individuals who are screened too frequently; at the same time in a low coverage of other population groups. Its effectiveness is limited and cost-effectiveness is poor.

The task of smear-taking for cytology and referring those with abnormal cytology to gynaecological services fits very well in the traditional preventive role of "health visitors". They can personally contact each woman who has been invited by the National Screening Registry, and encourage them to accept the offered screening. They can pay particular attention to those who have never attended a screening test, and to the less educated ones of lower socioeconomic status. They can easily provide pre-screening information on both the benefits and potential harms of screening, while assisting them to gain informed decision to participate. They can arrange mutually suitable appointment. Most importantly, they can take the cervical smears for cytology, and send it to cytology laboratories. After acquiring the test results, they can reassure the woman if the test is negative, and, in case of non-negative result, they can explain what "abnormality" means, and must refer the woman to gynaecological services for further examination (including colposcopy). Last but not least, they can offer psychological support to those who receive "bad news".

Ultimately, one can conclude that for the time being, cytology has remained the standard method of population screening for cervical cancer in Hungary. However, not only the strengths but also the limitations of cytology for cervical cancer screening must be recognised.

As far as the value of conventional cytology is concerned, there is room for criticism. Cytology is a subjective test, and in programmes without quality assurance, it is impossible to achieve and maintain its proper performance. Cytology is labour intensive; a great number of trained prescreener cytotechnologists and cytopathologists are required to be employed to meet the needs of a country-wide mass screening. Despite the low cost of consumables, high-quality cytology is expensive in absolute terms and may not be the most cost-effective option for screening [26]. Furthermore, as opposed to conventional cytology, liquid-based cytology has logistical and operational advantages (interpretation at higher speed, lower rate of unsatisfactory smears, and possibility of ancillary molecular testing using remnant fluid), but is more expensive, and neither more sensitive nor more specific than conventional cytology with respect to detection of histologically confirmed high-grade CIN [27].

Finally, the needs of populations vaccinated against HPV-16/18 have to be taken in consideration. In this case, we should anticipate that the positive predictive value (PPV) of cervical screening will be reduced because there will be fewer high-grade lesions among women with cytological abnormalities. It is therefore rational to develop multiple modalities for cervical cancer prevention, including methods that achieve similar or better screening performance than cytology alone, but also meet the demands of underserved populations, such as low cost, the need for fewer visits (i.e. cytology, diagnostic colposcopy, and treatment) in each screening cycle, and fewer interventions in a lifetime due to a grater negative reassurance of a single screening intervention [28].

Conclusion

The current state of conventional, morphology-based cervical screening as a public health measure calls for a "shift of paradigm of screening" for the sake of the female population. The insistence by the gynaecological community on their "historical role" seems to be a major obstacle. The "bad habits die hard". The notion of "gynaecological cancer screening" needs to be dismissed forever (because of negative psychological connotation of mentioning "can-

cer"), and instead become "cervical screening" which should come into general use. It is hoped that higher compliance with the offered screening would be attained through the involvement of the country-wide network of health visitors into the organized screening, and the ultimate aim of cervical screening programme: the improvement of women's health in the country be achieved in Hungary.

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