EuroMed Cancer Network contributions to eliminating cervical cancer in low- and middle-income Mediterranean countries

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Abstract

Background: Cervical cancer places a significant burden on low- and middle-income countries (LMICs). The EuroMed Cancer Network (EuMedCN) brings together cancer experts and stakeholders from the Mediterranean countries to promote sustainable cancer screening and support implementation of the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem.

Aim: To highlight the constructive role of EuMedCN in mitigating inequalities in access to cervical cancer prevention and screening across the Mediterranean LMICs.

Methods: Through its workshops and meetings, EuMedCN members discussed new developments in cancer prevention and control, and how best to translate the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem into public health policies in the Mediterranean LMICs. This led to targeted actions in the selected countries.

Results: Seven priority actions were implemented to improve cervical cancer screening in the Mediterranean LMICs. EuMedCN supported organized screening, new pilot technologies and enhancement of evaluation systems. Integrating cervical cancer screening into other disease programmes and fostering multidisciplinary networks were promoted as key to achieving targets of the WHO global strategy.

Conclusion: International networks, such as EuMedCN, have the potential to bring together experts and stakeholders to share experiences and catalyse resource mobilization. They can support affordable and synergistic solutions for cervical cancer prevention.

Keywords: Cervical cancer, screening, prevention, World Health Organization, Mediterranean, low- and middle-income countries, networking, EuroMed Cancer Network

Background: Cervical cancer is the fourth most common cancer among women globally, with an estimated 604,000 new cases and 342,000 deaths during 2020 (1). About 90% of new cases and deaths occur in low- and middle-income countries (LMICs) (2).

High mortality in LMICs is largely due to poor access to prevention, diagnosis, and treatment (2). Primary [human papillomavirus (HPV) vaccine] and secondary (screening) prevention of cervical cancer have been proven to be effective but these are not being equitably implemented (2). According to the World Health Organization (WHO), in May 2020, less than 25% of LMICs introduced the HPV vaccine into their national immunization schedules, compared to over 85% of high-income countries (HICs) (3). In LMICs, many screening activities remain opportunistic, or with limited planning and coverage, incorrect target populations, low participation, and resource misallocation (3,4). As for treatment, more than 90% of HICs reported the availability of public cancer treatment and palliative care, compared to around 30% of LMICs (3).

In November 2020, WHO launched the “Global Strategy to Accelerate the Elimination of Cervical Cancer” (hereafter “the Global Strategy”) (5). The Global Strategy set 3 targets to be reached by 2030: 1) 90% coverage of HPV vaccination among girls aged 15 or older; 2) 70% of women screened with a high-quality HPV screening test by the age of 35 and again by the age of 45; and 3) 90% of women with cervical pre-cancer or invasive cancer treated (3).

Achieving these goals is challenging in the Mediterranean region, where pronounced disparities in cervical cancer control have been observed between European Union (EU) HICs, and non-EU LMICs. However,
common cultural attitudes and behaviours exist across the region, therefore, international networks that bring together policymakers and healthcare professionals working towards shared cervical cancer control strategies can play a supporting role in promoting WHO policies in the region. The EuroMed Cancer Network (EuMedCN) has been playing this role since 2010, by convening cancer prevention experts and national health authorities from EU Mediterranean countries (France, Italy, and Spain), and non-EU Mediterranean countries (Albania, Bosnia and Herzegovina, Montenegro, and Serbia), as well as other Mediterranean States (Egypt, Jordan, Lebanon, Morocco, State of Palestine, the Syrian Arab Republic, and Türkiye) (5).

This paper highlights the inequalities in the cervical cancer burden and in access to screening across Mediterranean LMICs, while highlighting the constructive role played by EuMedCN toward implementing the Global Strategy. The paper also provides an insight into the brainstorming process among EuMedCN members for identifying achievable strategies to improve cervical cancer screening access for Mediterranean women.

Methods
EuMedCN members met regularly to update the Mediterranean region’s cancer screening framework, during which time new developments in cancer prevention and control were discussed, and best ways to translate WHO guidance into public health policies debated. From 2010 to 2019, EuMedCN organized annual workshops, but from 2020, in-person meetings were precluded due to the global COVID-19 pandemic. EuMedCN gatherings were therefore moved online, where the exchange of views on how to support the implementation of the Global Strategy continued. Focus was on the challenges and actions to overcome them based on the availability of state-of-art cervical cancer epidemiology and screening in the area.

Results and discussion

Cervical cancer burden and access to cancer screening in EuMedCN countries
Notwithstanding their common geographical origin, EuMedCN countries greatly differ in demographic and economic indices (Table 1). These discrepancies are reflected in their cervical cancer epidemiology (Table 1) (6). Modest age-standardized incidence rates (ASIR) were found in countries overlooking the northern African coast (ASIR <10 per 100 000), while a higher burden (ASIR ≥14 per 100 000) was observed in the Eastern European area. Incidence and mortality are particularly high in Bosnia and Herzegovina, Montenegro, and Serbia, with a severe 5-year prevalence and a considerable burden on health services. Despite lower incidences recorded in Morocco and Algeria, the higher mortality experienced in those countries reflects the limited access to effective diagnosis and treatment. A lack of, or poor quality, data was also common, necessitating caution in comparisons and hindering the planning of nationwide interventions (6).

Most recent WHO data on cervical cancer screening implementation in the region are summarized in Table 2. Although some organized cervical cancer screening was declared by most countries, population coverage was low (less than 50% of women tested), except for Türkiye and Lebanon. Several countries had fragmented implementation, with multiple underserved areas or subgroups.

EuMedCN countries differed regarding the screening test offered: Albania, Montenegro, and Türkiye offered HPV tests while Bosnia and Herzegovina, Lebanon, Serbia, the Syrian Arab Republic, and Tunisia offered pap smear. Morocco offered visual inspection with acetic acid (VIA) (7).

We found additional reasons for this low cervical cancer screening coverage in scientific literature, including limited cervical cancer knowledge among healthcare professionals and women, the stigma associated with sexually transmitted infections, and other cultural and religious barriers (8).

The EuMedCN roadmap for reaching WHO targets in Mediterranean LMICs
EuMedCN agreed on the following 7 priority actions for the practical application of the Global Strategy for cervical cancer screening:

1. Favouring organized screening. Both organized and opportunistic screenings have been associated with a decline in cervical cancer incidence and mortality, but decreases were lower and less cost-effective with opportunistic approaches (9). Organized programmes facilitate coverage of the entire eligible population, reducing inequalities and allowing for the monitoring and evaluation of the whole process (9,10). Opportunistic approaches are more likely to result in variability in screening quality and would rarely reach the entire eligible population, highlighting access disparities due to socio-demographic differences, with consequent limited coverage among high-risk groups or in underserved areas (9,10).

Despite the clear advantages of an organized approach, its implementation is not easy, it requires robust system infrastructure [e.g. updated information systems, interconnected facilities and laboratories, quality assurance (QA) mechanisms] and a strong commitment by policymakers (11). The availability of accessible municipal archives is essential to identifying and inviting the target population to attend screenings, which can be difficult in LMICs that lack updated population data. Where similar registries are not available or are incomplete, alternative solutions need to be determined. Shared knowledge
and experiences among EuMedCN members can be useful for identifying new approaches. For example, using vaccination datasets to create screening invitation data (as successfully conducted in Morocco) can be a worthwhile option.

Besides the approaches adopted by the national health services (opportunistic or organized), the private sector has a large impact on cervical cancer screening activities. Since standardization and monitoring is stricter in private facilities and out-of-pocket costs are relevant, equity and QA mechanisms can be more readily achievable than within the public health system (9).

**EuMedCN recommendations and actions:** EuMedCN encourages the implementation of organized cervical cancer screening programmes within the public health sector. The Network can offer support for the roll-out of effective programmes, proposing affordable solutions to enhance existing services and processes monitoring, and in adapting international guidelines locally.

### 2. Piloting new cervical cancer screening technologies.

Among Mediterranean LMICs, simple cervical cancer screening algorithms need to be introduced, adapting international recommendations to local peculiarities and/or finding new approaches. Cytology in LMICs was often unsuccessful, due to difficulties in establishing and maintaining testing quality and the long time needed for cytologist training (12,13). Although VIA has been long applied in LMICs as primary screening, since it is inexpensive and does not require laboratory services, this method presents low specificity, reproducibility, and sensitivity in post-menopausal women and in detecting endo-cervical dysplasia (14).

HPV testing is currently recommended as primary screening by WHO, as it is more effective than pap smear in detecting cervical intraepithelial neoplasia of grade 2 or worse (CIN2+) for women over 30 years, allowing for longer screening intervals (5 years or more) (15). Notwithstanding these advantages, this technique has certain intrinsic properties (i.e. infrastructure requirements, management of positive women, and costs) to be carefully considered (15).

Regarding logistics and affordability, promising new outcomes arose from self-
sampling (16). This option, where women collect their own specimen, is as accurate as physician-collected cervical scrapes (both in sensitivity and specificity), is cost-effective, and overcomes certain widespread barriers such as the limited availability of healthcare professionals and the reluctance of women to undergo gynecological examinations (16). Within EuMedCN, favorable experiences with self-sampling have been reported in Albania.

Managing the processes for women with positive HPV tests (for either self-sampling or healthcare professional sampling) can be demanding in LMICs. In HICs, for all HPV-positive women, pap smear is used as a triage for referring them either for a colposcopy or watchful follow-up after 1 year (15). Triage is used to avoid unnecessary treatments, and can be performed on the same HPV-testing sample (reflex testing) to avoid the need for multiple visits (15). This strategy is successfully being implemented in some EuMedCN countries, such as Türkiye, where cervical cancer screening is more structured (17). However, proposing cytology as a triage to all EuMedCN countries is not feasible, due to the unavailability of local cytology laboratories (15). Alternative triage techniques need to be tested in LMICs, and EuMedCN can offer an enriching platform for this.

Current research reports the availability and affordability of molecular triage reflex testing, which relies on HPV onco-protein detection and methylation of viral and host genes necessary for progression (18,19). Several of these methods can be easily performed because they do not require advanced infrastructure and should be piloted to evaluate their effectiveness, feasibility, and affordability.

Since women who test positive during triage are referred for a colposcopy, this step can create a bottleneck in LMICs, where well-equipped facilities and trained healthcare professionals are lacking. In this regard, EuMedCN can contribute by delivering high-quality training. New technologies, such as the evaluation of dysplastic lesions by image taking and artificial intelligence (AI), can also play a key role in ensuring quality enhancement by supporting healthcare professionals’ decisions in under-served areas (20).

### EuMedCN recommendations and actions:
EuMedCN supports HPV testing as a primary screening method for the eligible population. EuMedCN promotes applied research on new screening tests, innovative diagnostic and treatment technologies within a strong network of collaborations, and a common quality approach. EuMedCN can provide guidance for testing new
screening algorithms and solutions, encouraging high-quality research and its straightforward application in clinical practice, thus spreading knowledge and experiences within the Network.

3. Implementing adequate monitoring and evaluation systems. Effective screening programmes require suitable information technology (IT) systems to monitor the entire process from invitation to treatment. Recent breakthroughs in digital technology could simplify the development of user-friendly systems, ensuring effective organization. Similar systems will enable regular monitoring of process and outcome indicators, allowing for improvement opportunities and supporting feedback to policymakers and healthcare professionals. Keeping track of the results will also satisfy the need for updated cervical cancer incidence and mortality information.

IT platforms should be integrated with local databases and healthcare systems to provide complete, updated, and accessible data of eligible women.

It is mandatory that IT systems have provisions for confidentiality and security, as data can be at risk when stored in poorly designed systems. This issue is rarely considered in LMICs, and needs a further boost from the legal, technological, medical, and societal perspectives. Issues to be addressed are manifold, including the lack of secure IT, absence of strong legal framework for data protection, and lack of dedicated staff who are skilled in data ethics (21).

EuMedCN recommendations and actions: EuMedCN intends to support local communities in establishing effective and secure IT systems for cervical screening management. The Network recommends the integration of data ethics into IT developments, creating multidisciplinary groups with the required skills.

4. Promoting QA mechanisms. QA is essential for screening, as it ensures effective and efficient services for women. QA allows the monitoring of screening implementation through measurable standards and benchmarks defined at each step, from invitation to treatment. International common indicators have been proposed for this purpose (22,23). However, many of them are not transposable to LMICs, as previous experiences highlighted sub-optimal quality and completeness of data collection in these settings (21). Therefore, the definition of a minimum set of shared processes and outcome indicators, for evaluation and cross-country comparisons, is essential in LMICs. A common concern in low-resource settings is that healthcare professionals are not tasked with collecting and providing data for the assessment of health processes (21). Improvements in collecting, processing, and analyzing data in LMICs should represent a key pathway to improving health outcomes and achieving equity (21-23). For this reason, offering training on data collection and interpretation for all professionals involved in screening is broadly required.

EuMedCN recommendations and actions: EuMedCN recommends 3 main tasks to promote QA: (a) identify a list of must-have, country-adapted indicators that allow stakeholders to estimate outcomes of planned interventions, as already achieved in other experiences (22); (b) improve the quality of data collection, promoting formative initiatives for stakeholders, data managers, and healthcare professionals; and (c) provide feedback on the results to all actors involved in screening, from policymakers to healthcare professionals and the women.

5. Integrating cervical cancer screening into a framework of combined multidisease services. This integration could contribute to increased screening efficacy; combining different steps of care, increasing synergies among healthcare providers and professionals, and strengthening their skills and knowledge (24). Implementation of the integrated approaches is in alignment with the WHO framework on integrated people-centered healthcare services and its objectives (3). A recent review of cancer screening in Malawi outlined how the integration of cervical cancer screening with other health services (e.g. reproductive or HIV care) had a positive impact on testing uptake (25).

Another similar integration favours a diagonal approach to care (26). Rather than focusing on disease-specific vertical programmes or on horizontal initiatives (addressing generic system constraints), a diagonal approach seeks to do both concurrently. Examples of positive experiences in integrating breast and cervical cancer screening under the umbrella of a maternal or reproductive health policy are available in India (27) and Morocco (28).

EuMedCN recommendations and actions: EuMedCN promotes the integration of cervical cancer screening into existing healthcare programmes, as a guarantee for sustainability and equity. EuMedCN intends to encourage coordination within and across sectors, avoiding compartmentalized management and improving the efficiency of services, while reducing overall costs.

6. Encouraging connection between screening and therapeutic systems. For successful screening, coverage in high population areas must be followed by the appropriate treatment of pre-invasive and invasive lesions (3). Comprehensive management is then required (i.e. surgery, radiotherapy, chemotherapy, palliative services etc.), while administration timelines are crucial for survival, quality of life, and disability prevention (3). In LMICs, continuity of care for all screened women needs major improvement. Offering a screening test without adequate treatment and follow-up would be ineffective, as extending the length of the disease without influencing survival is an unethical option. A multidisciplinary approach is needed to ensure access to the entire diagnostic and care pathway to screened women, which goes beyond therapy and concerns the entire screening process and all the healthcare professionals involved (epidemiologists, laboratory staff, midwives, nurses, gynecologists, pathologists, etc.).
EuMedCN recommendations and actions: EuMedCN suggests to: (a) engage clinicians during the entire process, creating multidisciplinary groups to ensure access to the entire diagnostic and care pathway to screened women; (b) encourage multidisciplinary discussions of case studies and screening results; (c) identify treatment services for screen-detected lesions, establishing clear and simple referral procedures; (d) train healthcare professionals regarding shared protocols and follow-up procedures; and (e) assure feedback mechanisms for women and healthcare professionals.

7. Promoting multicentre and multidisciplinary local networks. Local multidisciplinary networks (at regional or national levels) can support their members with the implementation and coordination of high-quality screening programmes, to gain the highest advantages with the lowest harms. These networks can also facilitate profitable exchanges about cancer care, scientific research, evidence-based screening implementation, and healthcare professionals' continued education and training. They can provide periodic updates on screening activities to policymakers, boosting both awareness and commitment. Further, an affiliation to international networks (such as EuMedCN) can provide comparable advantages on a wider scale, favouring cross-country comparisons and collaborations. Regarding cervical cancer screening, national and international networks, like the Union for the Mediterranean (UfM), promote gender-sensitive services and interventions aimed at women's empowerment (29). Engaging women's advocacy groups and associations can also be relevant for promoting cancer prevention awareness.

EuMedCN recommendations and actions: EuMedCN recommends the creation and strengthening of multidisciplinary local and international networks, which play a catalyzing role for affordable and synergistic solutions in cervical cancer prevention. Moreover, EuMedCN, in close collaboration with organizations promoting women's rights and local advocacy groups, aims to enhance the target population's awareness of and empowerment about cervical cancer prevention.

Conclusions
Achieving the Global Strategy's goals is challenging, especially in LMICs, as it requires significant resources and wider involvement and awareness among researchers, policymakers, and advocacy groups.

However, it must be noted that the Global Strategy was adopted during the COVID-19 pandemic, which posed additional, severe challenges to preventing cancer deaths, including the interruption of vaccination, screening, and treatment services (30). Current actions planned in line with the Global Strategy have been slowed down or blocked (30,31). Despite this, WHO urges all countries to ensure that, to the extent possible, vaccination, screening, and treatments continue safely and with all necessary precautions (3). Notwithstanding the difficulties of the period, EuMedCN continued brainstorming toward the achievement of the Global Strategy goals and provided 7 priority actions, including common recommendations and tasks suggested for Mediterranean LMICs. These actions are conceived as part of a multilevel working plan, bringing together key actors and stakeholders who can contribute to implementing sustainable initiatives for upgrading cervical cancer screening in the region.

EuMedCN can act as a promoter of collaborations among countries, improving the sharing of knowledge and the development of sustainable and high-quality cervical cancer screening programmes. The Network can encourage ongoing research; professional updates; and the endorsement of cancer prevention in local cultures through close collaboration with local organizations, advocacy groups and healthcare professionals. In this regard, international co-operation, such as with WHO, can play a valuable role in fostering connections between HICs and LMICs.

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مساهمات الشبكة الأورومتوسطية المعنية بالسرطان في القضاء على سرطان عنق الرحم في بلدان الشرق المتوسط المخفضة والمتوسطة الدخل

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الخلاصة

الخليفة: يُلقِّي سرطان عنق الرحم عبأً كبيرًا على البلدان المخفضة والمتوسطة الدخل. وتجمع "الشبكة الأورومتوسطية المعنية بالسرطان (EuMedCN)" خبراء السرطان وأصحاب المصلحة من بلدان الشرق المتوسط لتعزيز الفحص المستدام للسرطان، ودعم تنفيذ الاستراتيجية العالمية من الصحة العالمية لتسريع وتحقيق القضاء على سرطان عنق الرحم. للأهداف: هدفت هذه الدراسة إلى تحليل الأدوات الرئيسية "الشبكة الأورومتوسطية المعنية بالسرطان" في عدد من أوجه عدم المساواة في الحصول على الوقاية من سرطان عنق الرحم وفحصه في بلدان الشرق المتوسط المخفضة والمتوسطة الدخل.

طرق البحث: نانش أعضاء "الشبكة الأورومتوسطية المعنية بالسرطان"، من خلال حلقات العمل والاجتماعات المتخصصة، التطورات الجديدة في مجال الوقاية من السرطان وفقًا لما تم تحديده في الاستراتيجية الدولية للصحة العالمية للقرن الخامس. ویرى اثر اتخاذ إجراءات مستهدفة في البلدان المختارة.

النتائج: نُفِّذت سبع إجراءات ذات أولوية لتحسين فحص سرطان عنق الرحم في بلدان الشرق المتوسط المخفضة والمتوسطة الدخل. ودعمت "الشبكة الأورومتوسطية المعنية بالسرطان" فحص المرض والخوارزميات الوراثية الجديدة، وتعزيز نظام التشخيص. وجرى التشجيع على دمج خدمات فحص سرطان عنق الرحم في برامج مكافحة الأمراض الأخرى، وتعزيز الشبكات المتنوعة للが始まات، بوصفها عنصرين أساسيين تحتوي غايات الاستراتيجية العالمية.

الاستنتاجات: يمكن للشبكات الدولية، مثل "الشبكة الأورومتوسطية المعنية بالسرطان"، أن تجمع الخبراء وأصحاب المصلحة لواجهة وتقدير نقاط القوة وتقدير نقاط القرب من سرطان عنق الرحم.

References


