

Brussels, 17 May 2024

COST 064/24

DECISION

Subject: Memorandum of Understanding for the implementation of the COST Action
“Mediterranean Cancer Screening and Early Diagnosis Network” (Medi-CaSE) CA23151

The COST Member Countries will find attached the Memorandum of Understanding for the COST Action Mediterranean Cancer Screening and Early Diagnosis Network approved by the Committee of Senior Officials through written procedure on 17 May 2024.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA23151
MEDITERRANEAN CANCER SCREENING AND EARLY DIAGNOSIS NETWORK (Medi-CaSE)

The COST Members through the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action, referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any document amending or replacing them.

The main aim and objective of the Action is to enhance cancer prevention, specifically for breast, cervical and colorectal cancers, by sharing best practices and fostering collaboration among both inexperienced and established programs in the Mediterranean area, with a specific focus on inclusiveness and gender equality. This will be achieved through the specific objectives detailed in the Technical Annex.

The present MoU enters into force on the date of the approval of the COST Action by the CSO.

OVERVIEW

Summary

Cancer burden (in particular for breast, cervical and colorectal cancer) represents a compelling issue worldwide, and the Mediterranean area is no exception. In this area, the implementation of cancer control policies is heterogeneous as most high-income countries set up organized programs, while low-middle-income countries (LMICs) face more constrained situations. Either way, a general enhancement, considering implementation, organization, monitoring and participation, is needed. Despite broad differences, commonalities, that go beyond geographical proximity, exist in relation to socio-cultural backgrounds, and they can be successfully exploited in defining common preventive approaches.

The Mediterranean Cancer Screening and Early Diagnosis Network (Medi-CaSE) aims to involve countries bordering the Mediterranean Sea, to foster health systems' capacities in the implementation of effective and sustainable secondary cancer prevention policies. Further, Medi-CaSE will form a common research platform in cancer screening, for investigating gaps in current knowledge with a specific attention to inclusiveness and innovation.

Medi-CaSE can be valuable in identifying research priorities, collecting best practices, spreading and translating evidence-based interventions into clinical practice. Meanwhile, training and career opportunities for local professionals and young researchers will be provided, favoring a multidisciplinary approach. All tasks will be carried out with the early involvement of local stakeholders and policymakers.

Medi-CaSE has been conceived to face several challenges, considering local scenarios of cancer secondary prevention and current epidemiological frameworks. Actual inquiries on this topic are hampered by fragmentation, limited participation from LMICs, and lack of large cross-countries' investigations. Medi-CaSE aims to deal with such issues, implementing joint experiences and limiting resource scattering.

| | |
|--|--|
| <p>Areas of Expertise Relevant for the Action</p> <ul style="list-style-type: none"> ● Health Sciences: Epidemiology | <p>Keywords</p> <ul style="list-style-type: none"> ● Breast cancer ● Cervical cancer ● colorectal cancer ● Early diagnosis ● Screening |
|--|--|

Specific Objectives

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination

- Creating an international and multidisciplinary joint network, gathering a well-balanced group of academics, researchers, epidemiologists, physicians, other HPs, statisticians, data managers, and stakeholders, for enhancing breast, cervical and colorectal cancer prevention across the Mediterranean Sea.
- Intensifying international collaborations for increasing knowledge regarding cancer secondary prevention in the area, by favoring expertise sharing.
- Exploiting the common Mediterranean socio-cultural background, for conceiving synergies and joint

solutions in cancer control (for the entire region or restricted geographical areas).

- Identifying the best practices for enhancing cancer early diagnosis/screening implementation and participation, to be proposed as models for similar contexts.
- Identifying barriers and facilitators to cancer prevention, considering the different contexts, retrieving common solutions to be explored and disseminated.
- Considering the sustainability and cost-effectiveness of different cancer prevention policies in selected contexts, investigating potential factors affecting their feasibility, and to consequently inform local policymakers and stakeholders.
- Sharing periodically results among involved parties (e.g. academics, researchers, health professionals, the general public, stakeholders and enterprises).
- Supporting the inclusion of cancer screening evidence-based findings into local health policies.

Capacity Building

- Providing multidisciplinary education and training opportunities on cancer prevention to local health professionals, programme and data managers, stakeholders and policymakers through the implementation of Training Schools, Short-term Scientific Missions, and other educational opportunities.
- Discussing and formulating common strategies for enhancing cancer prevention awareness and participation in screening in the general population with specific attention to vulnerable groups.
- Promoting the involvement and the career opportunities of young professionals, especially in underserved contexts, favoring their participation and leadership skills in the newly formed research groups.
- Promoting gender-balance in all the capacity building actions, aiming to achieve at least 50% of female participants in each task.
- Encouraging geographically balanced representativeness within the Network and its activities. The COST Action aims, in the long-term, to include representatives from all the Mediterranean countries. In particular, in all activities, the involvement of at least 50% of participants from Inclusiveness Target Countries will be ensured.
- Engaging main advocacy groups and citizens' associations to support and guide the focus on immigration issues among Mediterranean countries making the cultural and social aspects of the countries of origin a pivotal factor in the successful integration of these populations into the new environments.
- Making available country-adapted road-maps for the enhancement of cancer prevention's infrastructures and services.

TECHNICAL ANNEX

1. S&T EXCELLENCE



"...We do not even know how far it extends: how wide stretches of the coastline it occupies, how far it goes into the indentations of the land and where it actually ceases. Ancient wisdom taught that our sea reaches as far as the olive tree grow. And yet this is not everywhere the case: there are places that lie right on the coast that are not Mediterranean or are less so than others that are more distant. The Mediterranean is not just geography. Its boundaries are not defined in either space or time. We do not know how to determine them and in what way: they are irreducible to sovereignty or history; they are neither state nor national. [...] On the Mediterranean, Europe was conceived."

Predrag Matvejević - Mediterranean Breviary - 1987

1.1. SOUNDNESS OF THE CHALLENGE

1.1.1. DESCRIPTION OF THE STATE OF THE ART

Cancer control is a pressing global public health concern, with a significant impact in low-and middle-income countries (LMICs), where the majority of cancer-related deaths occur in regions like Africa, Asia, and Central and South America [1,2]. The Mediterranean area, which includes both high-income countries (HICs) and LMICs, is also affected by cancer, including breast (BC), cervical (CC), and colorectal cancer (CRC) (Table 1) [3]. The cancer burden in this region is expected to increase in the coming years, particularly in LMICs, due to demographic changes and the adoption of unhealthy western lifestyles, such as poor diets and reduced physical activity, leading to rising rates of overweight and obesity. These trends have been steadily increasing in the Mediterranean region since 2000 [4].

The implementation of cancer control policies in the Mediterranean region, especially in LMICs, faces numerous challenges, including weak commitment from policymakers, fragmented local health services, limited resources and funding, and restricted access to cancer services and drugs [5,6]. Political instability in some countries has further hindered cancer services.

In contrast, HICs in the region have well-established cancer control actions, but there's a need for improvement, especially in reaching vulnerable subgroups like migrants. Migrants, who often use the Mediterranean as a migration route, present unique challenges and epidemiological outlines in the fight against cancer [7]. Despite differences in population profiles, commonalities based on sociocultural backgrounds can be leveraged to establish shared cancer prevention strategies [8].

Cancer early detection is crucial for improving the chances of successful treatment and reducing the need for invasive procedures. There are two primary components of early detection: early diagnosis and screening [9,10]. Early diagnosis involves identifying cancer in individuals who display symptoms of the disease. This approach is broadly applicable to various types of cancer and clinical settings, with the goal of down-staging the disease. On the other hand, screening aims to detect cancer at a preclinical stage in individuals who do not show any symptoms. However, it is a complex process that requires significant financial investments and a robust healthcare infrastructure to ensure that all screen-detected lesions are promptly diagnosed and treated. It's important to note that cancer screening is not a one-time examination; it involves multiple rounds at different intervals [10,11].

Currently, there is strong evidence supporting the implementation of organized, quality-assured, population-based screening programs for breast (BC), cervical (CC) and colorectal cancer (CRC) in countries where these diseases are recognized as significant public health issues, provided that the necessary resources and healthcare systems are in place to deliver effective and timely diagnostic and therapeutic services [11,12].

On the contrary, poorly screening initiatives can be counterproductive and lead to the inefficient use of resources. In such cases, it is advisable to focus on awareness campaigns and early diagnosis programs as more suitable options.

However, only a few of these programs meet all the requirements to be considered as population-based. Indeed, most activities remain opportunistic, with limited planning and monitoring. This can lead to high costs and inefficiencies. Moreover, often these initiatives are local/regional, and only a limited proportion of the eligible population is effectively covered [12,13]. Furthermore, poor awareness and false beliefs can leverage citizens' participation [14].

Recently, global commitments proposed by the World Health Organization (WHO) "Global Non-Communicable-Diseases Action Plan 2013-2030" highlighted the importance of early detection and treatment of non-communicable diseases for rapidly reducing the burden of premature mortality [14]. As examples, WHO launched a call for action to eliminate CC as a public health problem based on three pillars (i.e. vaccination, screening and treatment) [15], and established the Global Breast Cancer Initiative (GBCI), bringing together stakeholders worldwide with the goal of reducing BC [16]. In addition, over the last decades, WHO and other international organizations developed comprehensive guidelines for the implementation and evaluation of effective cancer control policies, including organizational tools for program managers and healthcare providers [17-19].

All countries should make use of this guidance to strengthen their cancer prevention activities, adopting evidence-based actions, while addressing financial, geographical, logistic and sociocultural barriers. However, often a straightforward translation of these documents into clinical practice is not feasible, requiring a local adaptation [21].

Finally, improving population awareness, stakeholders' commitment, and healthcare professionals' (HPs) knowledge and skills regarding cancer secondary prevention are key components of a comprehensive enhancement strategy [22].

From here on, the term "cancer secondary prevention" mainly refers to BC, CC and CRC early diagnosis and screening.

Table 1. Cancer epidemiology background in Mediterranean countries

| Location | BREAST CANCER | | | CERVICAL CANCER | | | COLORECTAL CANCER | | |
|------------------------|---|---|--------------------------------------|---|---|--------------------------------------|--|--|--------------------------------------|
| | Estimated age-standardized incidence rates in 2020, females, all ages | Estimated age-standardized mortality rates in 2020, females, all ages | Mortality Incidence rate ratio (MIR) | Estimated age-standardized incidence rates in 2020, females, all ages | Estimated age-standardized mortality rates in 2020, females, all ages | Mortality Incidence rate ratio (MIR) | Estimated age-standardized incidence rates in 2020, both sexes, all ages | Estimated age-standardized mortality rates in 2020, both sexes, all ages | Mortality Incidence rate ratio (MIR) |
| Albania | 48.3 | 11.4 | 0.24 | 6.6 | 3.3 | 0.50 | 7.7 | 3.8 | 0.49 |
| Algeria | 55.8 | 18.5 | 0.33 | 25.6 | 4.5 | 0.18 | 15.3 | 8.3 | 0.54 |
| Arab Republic of Egypt | 48.7 | 20.4 | 0.42 | 2.9 | 1.7 | 0.59 | 6.1 | 3.4 | 0.56 |
| Bosnia and Herzegovina | 52.4 | 15.7 | 0.30 | 14.3 | 5.2 | 0.36 | 27.0 | 14.5 | 0.54 |
| Croatia | 69.3 | 14.6 | 0.21 | 10.1 | 3.2 | 0.32 | 36.3 | 19.6 | 0.54 |
| Cyprus | 82.0 | 17.8 | 0.22 | 5.6 | 2.9 | 0.52 | 24.3 | 10.7 | 0.44 |
| France | 99.1 | 15.6 | 0.16 | 7.0 | 2.2 | 0.31 | 30.1 | 10.4 | 0.35 |
| Greece | 71.9 | 14.5 | 0.20 | 8.0 | 2.2 | 0.28 | 26.9 | 10.7 | 0.40 |
| Israel | 78.3 | 16.7 | 0.21 | 4.9 | 2.0 | 0.41 | 21.9 | 9.0 | 0.41 |
| Italy | 87.0 | 13.4 | 0.15 | 6.9 | 1.6 | 0.23 | 29.3 | 10.1 | 0.34 |
| Jordan | 59.5 | 19.7 | 0.33 | 2.9 | 1.9 | 0.66 | 17.7 | 9.6 | 0.54 |
| Lebanon | 54.8 | 19.9 | 0.36 | 3.4 | 2.0 | 0.59 | 12.2 | 6.7 | 0.55 |
| Libya | 34.6 | 14.3 | 0.41 | 7.7 | 4.9 | 0.64 | 15.7 | 10.2 | 0.65 |
| Malta | 89.5 | 11.5 | 0.13 | 3.7 | 1.1 | 0.30 | 25.7 | 10.1 | 0.39 |
| Montenegro | 72.3 | 23.9 | 0.33 | 26.2 | 10.5 | 0.40 | 27.4 | 13.7 | 0.50 |
| Morocco | 56.4 | 17.5 | 0.31 | 10.4 | 5.8 | 0.56 | 9.9 | 6.2 | 0.63 |
| Palestinian Authority | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| Serbia | 86.8 | 23.9 | 0.28 | 18.7 | 7.9 | 0.42 | 33.6 | 16.7 | 0.50 |
| Slovenia | 69.2 | 13.4 | 0.19 | 6.7 | 2.4 | 0.36 | 39.6 | 11.7 | 0.30 |
| Spain | 77.5 | 10.6 | 0.14 | 5.4 | 1.6 | 0.30 | 35.8 | 11.5 | 0.32 |
| Syrian Arab Republic | 57.1 | 26.2 | 0.46 | 2.8 | 1.9 | 0.68 | 12.9 | 8.2 | 0.64 |
| Tunisia | 41.4 | 12.5 | 0.30 | 4.6 | 2.4 | 0.52 | 12.7 | 6.4 | 0.50 |
| Turkey | 46.6 | 12.9 | 0.28 | 4.8 | 2.2 | 0.46 | 20.6 | 10.1 | 0.49 |

1.1.2. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

The implementation of early diagnosis and/or screening programs for BC, CC, and CRC varies substantially across the Mediterranean Sea [13-15]. Considering the current complex scenario of cancer secondary prevention in the Mediterranean Region (see table 1), a network of experts including representatives from this area can be beneficial to foster health systems' capacities for enhancing effective and sustainable cancer prevention policies. This is the core mission of the **Mediterranean Cancer Screening and Early Diagnosis Network (Medi-CaSE)**, an international and multidisciplinary network gathering researchers, health care providers, and stakeholders like advocacy groups, non-Governmental organizations (NGOs), and small-and medium-sized enterprises (SMEs). Medi-CaSE will act as a platform for cross-countries research coordination, allowing to identify areas of common interest with a specific focus on inclusiveness and gender equality, fostering interdisciplinary collaborations and boosting careers for young researchers in early diagnosis and screening. Medi-CaSE, up to our knowledge, will be the first COST Action devoted to cancer secondary prevention in the Mediterranean area. It can play a crucial role in: 1) collecting best practices from participants; 2) spreading and translating evidence-based interventions into local contexts and current clinical practice; 3) sharing

knowledge and experiences among professionals; 4) actively involving local stakeholders, HPs and policy-makers.

All benefits are intended to be bi-directional, as those countries with cancer control policies at initial stages will benefit from the direct support of more experienced ones, while those with structured and well-established programs will learn from experiences in LMICs, encouraging a re-evaluation process and/or a further enhancement, especially considering the involvement of vulnerable populations.

1.2. PROGRESS BEYOND THE STATE OF THE ART

1.2.1. APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE OF THE ART

The core mission of Medi-CaSE derives from the pressing need to tackle cancer secondary prevention in the entire Mediterranean area, where multiple and diverse demands coexist [11-14]. Tables 2,3,4, which summarize the state of the art of cancer screening among countries currently accepted to join the network, underline the heterogeneity of the context. Medi-CaSE can facilitate the collection and analysis of these data in order to obtain a more complete view of the implementation and organization status of cancer early detection in the Mediterranean area.

The main issues to be taken into account when facing the complex scenario of cancer secondary prevention are: the shortage of evidence-based findings from low-resource settings, the need of adapting international recommendations to local contexts and translating them into clinical practice, the demand of finding innovative solutions for enhancing cancer secondary prevention awareness and participation in the eligible population, the need of testing and applying new technology advancements for improving screening processes, and the urgency of implementing sustainable and effective cancer prevention services and evaluation systems [12-23].

Table 2. Information about breast cancer screening programs in country members

| Location | Presence of national screening programs for breast cancer (Y/N) | Type of screening (O=organized; OPP=opportunistic) | Starting year of the program | Target population (age) | Screening test | Screening interval (years) |
|------------|---|--|------------------------------|-------------------------|----------------|--------------------------------|
| Albania | Y | OPP | 2021 | 50-60 | Mammography | 2 |
| Cyprus | Y | O | 2009 | 50-69 | Mammography | 2 |
| Greece | N | OPP | 1990 | 35-80 | Mammography | 1 - 2 |
| Italy* | Y | O | 1992 | 45-74 | Mammography | 1 (for 45-49) 2 (for 50-74) |
| Jordan | Y | OPP | 2007 | 40-60 | Mammography | 1 |
| Lebanon | Y | O | 2002 | 40+ | Mammography | 1 |
| Malta | Y | O | 2009 | 50-69 | Mammography | 2 |
| Montenegro | Y | O | 2002 | 40+ | Mammography | 1 |
| Serbia | Y | O | 2013 | 50-69 | Mammography | 2 |
| Slovenia | Y | O | 2008 | 50-69 | Mammography | 2 |
| Spain | Y | O | 1990 | 50-69 | Mammography | 2 |

* Organization and screening protocols may change by regions.

Table 3. Information about cervical cancer screening programs in country members

| Location | Presence of national screening programs for cervical cancer (Y/N) | Type of screening (O=organized; OPP=opportunistic) | Starting year of the program | Target population (age) | Screening test | Screening interval (years) |
|------------|---|--|---|-------------------------|---|------------------------------|
| Albania | Y | O | 2019 | 40-50 | HPV test | 5 |
| Cyprus | Y | O | 2016 | 25-43 | Pap Test | 3 |
| Greece | N | OPP | 1990 | 18-65 | Pap Test | 2 - 3 |
| Italy* | Y | O | 1992 | 25-64 | Pap test (25-29) HPV test (30-64) | 3 (Pap test) 5 (HPV test) |
| Jordan | N | OPP | | Maternity age | Pap test | |
| Lebanon | N | OPP | | | | |
| Malta | Y | O | 2016 | 25-43 | Pap test | 3 |
| Montenegro | N | OPP | | | | |
| Serbia | Y | O | 2013 | 25-64 | Pap test | 3 |
| Slovenia | Y | O | 2003 | 20-64 | Pap test with HPV triage | 3 |
| Spain | Y | OPP; transitioning to O by 2029 | 2006 national recommendation 2019 inclusion of HPV testing & starting the implementation of the organized programme | 25-65 | Pap test/HPV test Transitioning from Pap test for 25-65 to Pap test for 25-29 & HPV test for 30-65 in Catalonia Region Pap test for 25-34 & HPV test for 35-65 in the rest of the regions | 3 (Pap test) 5 (HPV test) |

* Organization and screening protocols may change by regions
HPV: Human Papilloma Virus

Table 4. Information about colorectal cancer screening programs in country members

| Location | Presence of national screening programs for colorectal cancer (Y/N) | Type of screening (O=organized; OPP=opportunistic) | Starting year of the program | Target population (age) | Screening test | Screening interval (years) |
|------------|---|--|------------------------------|-------------------------|----------------|----------------------------|
| Albania | Y | O | 2015 | 40-70 | gFOBT | 1 |
| Cyprus | Y | O | 2013 | 56-74 | FIT | 2 |
| Greece | N | | | | | |
| Italy* | Y | O | 2006 | 50-69 | FIT | 2 |
| Jordan | N | | | | | |
| Lebanon | N | OPP | | | | |
| Malta | Y | O | 2013 | 56-74 | FIT | 2 |
| Montenegro | N | OPP | | | | |
| Serbia | Y | O | 2013 | 50-74 | FIT | 2 |
| Slovenia | Y | O | 2009 | 50-74 | FIT | 2 |
| Spain | Y | O | 2006 | 50-69 | FIT | 2 |

* Organisation and screening protocols may change by regions

gFOBT: guaiac Fecal Occult Blood Test
FIT: Faecal Immunochemical Test

In this respect, the main elements of Medi-CaSE allowing to move beyond the current situation are:

- establishment of a multidisciplinary network (researchers, HPs and other interested parties) for sharing knowledge and experiences on cancer secondary prevention in several Mediterranean countries;
- providing training opportunities, including Training Schools (TS) and other educational opportunities (in-person and online) for local professionals involved in cancer prevention;
- dissemination of best practices and guidelines, encouraging local adaptation of international recommendations;
- defining essential steps and prerequisites for efficient early diagnosis and cancer screening services, with a focus on sustainability and equitable access, addressing barriers for vulnerable groups;
- creating and sharing a set of indicators for the monitoring and evaluation of cancer secondary prevention, facilitating cross-countries comparisons and data interpretation training;
- active engagement of local community stakeholders and advocacy groups to identify common cancer prevention and awareness initiatives to be spread in the Mediterranean region; for reaching this objective, a parallel stakeholders network will be created for the dissemination of MEDI-CaSE actions among this group;
- identifying ongoing research projects in cancer screening, highlighting gaps and opportunities for collaborative projects and cross-country interventions, including innovative strategies (as self-sampling for CC screening) for involving underserved groups.

1.2.2. OBJECTIVES

1.2.2.1. Research Coordination Objectives

Considering Research Coordination, main objectives of Medi-CaSE are:

- Creating an international and multidisciplinary joint network, gathering a well-balanced group of academics, researchers, epidemiologists, physicians, other HPs, statisticians, data managers, and stakeholders, for enhancing BC, CC and CRC prevention across the Mediterranean Sea.
- Intensifying international collaborations for increasing knowledge regarding cancer secondary prevention in the area, by favoring expertise sharing.
- Exploiting the common Mediterranean socio-cultural background, for conceiving synergies and joint solutions in cancer control (for the entire region or restricted geographical areas).
- Identifying the best practices for enhancing cancer early diagnosis/screening implementation and participation, to be proposed as models for similar contexts.
- Identifying barriers and facilitators to cancer prevention, considering the different contexts, retrieving common solutions to be explored and disseminated.
- Considering the sustainability and cost-effectiveness of different cancer prevention policies in selected contexts, investigating potential factors affecting their feasibility, and to consequently inform local policymakers and stakeholders.
- Sharing periodically results among involved parties (e.g. academics, researchers, HPs, the general public, stakeholders and enterprises),
- Supporting the inclusion of cancer screening evidence-based findings into local health policies.

1.2.2.2. Capacity-building Objectives

Capacity building will consider both HPs and institutional expertise at a national and an international level. In this field, the main objectives of Medi-CaSE are:

- providing multidisciplinary education and training opportunities on cancer prevention to local HPs, programme and data managers, stakeholders and policymakers through the implementation of TS, - Short-term Scientific Missions (STMS), and other educational opportunities;
- discussing and formulating common strategies for enhancing cancer prevention awareness and participation in screening in the general population with specific attention to vulnerable groups;
- promoting the involvement and the career opportunities of young professionals, especially in underserved contexts, favoring their participation and leadership skills in the newly formed research groups;
- promoting gender-balance in all the capacity building actions, aiming to achieve at least 50% of female participants in each task;
- encouraging geographically balanced representativeness within the Network and its activities. The COST Action aims, in the long-term, to include representatives from all the Mediterranean countries. In particular, in all activities, the involvement of at least 50% of participants from ITCs will be ensured;
- engaging main advocacy groups and citizens' associations to support and guide the focus on immigration issues among Mediterranean countries making the cultural and social aspects of the countries of origin a pivotal factor in the successful integration of these populations into the new environments;
- making available country-adapted road-maps for the enhancement of cancer prevention's infrastructures and services.

2. NETWORKING EXCELLENCE

2.1. ADDED VALUE OF NETWORKING IN S&T EXCELLENCE

2.1.1. ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

Medi-CaSE Network can provide the following added values in relation to the existing European and international efforts.

1. Implementation of cross-countries research projects

Several international investigations worked on elaborating, implementing and evaluating cancer prevention interventions [18-29]. However, up-to-date, these inquiries are severely hampered by the fragmentation of experiences, the limited participation of professionals from LMICs, and the lack of large cross-countries' collaborations. Medi-CaSE aims to directly deal with these issues, offering a hub to address cancer prevention implementation and research across the Mediterranean. The large engagement within Medi-CaSE of members from Inclusiveness Target Countries (ITCs) aims to foster the implementation of cross-countries research projects to identify commonalities and differences, and infer from these. Accounting for difficulties to access research funding in cancer prevention, especially in LMICs, Medi-CaSE can be valuable for the definition of shared research priorities and advantageous participation in common calls, avoiding the scattering of resources.

2. Supporting the adoption/adaptation of International Guidelines and recommendations

International guidance for cancer early diagnosis and screening implementation are currently available (e.g. WHO, European Commission guidelines), but often they are not simply transposable in all contexts, as needing local adaptations accounting for socio-economic and organizational features [11,12,19]. Medi-CaSE will be in an ideal position for disseminating these documents, as well as to support local adaptation processes and their direct translation into clinical practice. In adapting guidance, consideration will be given to: local evidence, such as specific health questions relevant to a local context of use; specific needs, priorities, legislation, policies and resources; scopes of practice within the local health services; and fit within existing models of delivery in the targeted setting.

3. Being in line with international cancer policies

The Action directly deals with the requirements defined in the EU Cancer Mission and Europe's Beating Cancer Plan, posing cancer as a European Commission's priority in health [24]. In this framework, the Action will fit well with the European Council recommendations recent update on cancer screening (November 2022) [25]. Among the others, these documents stated the following recommendations:

- Provide evidence-based, person-centered cancer screening.
- Implement accessible screening programs following the most updated European guidelines.

- Develop 'risk-stratified cancer screening' protocols and monitor outcomes.
- Train personnel for high-quality services.
- Ensure equitable access, including marginalized groups.
- Guarantee screening access for people with disabilities.

Medi-CaSE actions respond to several of these matters, fostering a close international collaboration that goes beyond the European borders. Indeed, Medi-CaSE tasks will support cancer screening evaluation and monitoring, as well as the screening accessibility of vulnerable populations, and the definition and straightforward translation of best practices into current clinical activities.

4. Guaranteeing gender balance and enhancing young researchers career opportunities

Medi-CaSE will ensure that actions are taken by integrating gender balance into all planning and operational strategies and activities. Moreover, Medi-CaSE will try to guarantee an adequate participation of junior and senior researchers in order to integrate the energy and enthusiasm that younger professionals can bring to the team with seniors' competences/knowledge.

5. Fostering the integration with the civil society

Medi-CaSE will encourage cooperation with civil society organizations in order to coordinate and integrate more inclusive cancer prevention activities in all the involved countries. Relevant stakeholders of the third sector can provide valuable inputs for designing integration policies that strengthen collaboration and dialogue locally. This encompasses the active consultation of civil society actors in defining objectives and actions, for example through consultative committees, informal meetings or collaboration and support in the implementation of research and cancer control policies. Benefits of cooperation with civil society groups can be practical in achieving short and long-term goals due to their greater capacities and additional knowledge and experience on the ground. Indeed, they are able to recognize local population needs and requirements, collaborating in tailoring cancer early diagnosis and screening services to multiple target groups.

2.2. ADDED VALUE OF NETWORKING IN IMPACT

2.2.1. SECURING THE CRITICAL MASS, EXPERTISE AND GEOGRAPHICAL BALANCE WITHIN THE COST MEMBERS AND BEYOND

Medi-CaSE joins different Mediterranean excellences and institutional representatives from EU- and non-EU Mediterranean countries, and NGOs. The network, involving high-level scientific and institutional centers, can guarantee the quality all along the process. The active involvement of all partners in several tasks strengthens a multidisciplinary approach to cancer control. All participants are selected for their leading role in cancer secondary prevention in their home countries and for providing a unique set of knowledge essential to elaborate and evaluate common cancer prevention pathways in the Mediterranean area. The network will be formed by Action members, from COST Full and cooperating Members, among them ITCs, and also from Near Neighbor Countries. To ensure the geographical balance, ITCs will be largely involved within Medi-CaSE from the beginning of the Action. Medi-CaSE will be open to expand and support the cross-border cooperation between COST Full Members and other Near Neighbor Countries bordering the Mediterranean Sea. There will be also representatives from other countries not directly bordering the Mediterranean coasts as members of Medi-CaSE. This will contribute to study differences or commonalities between Mediterranean and other countries. The further enlargement is expected as part of the Action.

Multidisciplinary approach is ensured by the engagement of different professional profiles. In addition, all participants have a consistent experience in research methodology, data analysis, team management, and resource planning, thus providing an ideal environment for multidisciplinary international collaborations and knowledge exchanges.

The engagement of further professional profiles and countries aims to increase the long-term multidisciplinary approach as well as the geographical representativeness. Indeed, from the Action initial phases, a great effort will be focused on the involvement of representatives from the Mediterranean Countries/Institutions not yet included. For the accomplishment of this task, local Ministries of Health, and International Organizations' representatives will be contacted. The contribution of already involved members will be paramount for enlarging the existing collaborations, adopting a chain-referral sampling. New members will be invited to join the Network, and for this purpose, Medi-CaSE website will represent a useful tool (see Section 3.2.2). This enlargement will be facilitated by the well-established experiences of many members in international studies and/or in ongoing cross-countries collaborations.

Furthermore, the Network will be committed to involve in its actions ongoing screening programmes and initiatives in participating countries, as well as all scientific societies representing relevant professionals.

2.2.2. INVOLVEMENT OF STAKEHOLDERS

A comprehensive stakeholders' engagement and communication plan will be devised to identify, involve, and communicate with key actors and groups in the Medi-CaSE network. This plan will ensure effective strategies and actions for engaging and gaining the support of stakeholders, including HPs, scientific communities, policymakers, community/religious leaders, NGOs, patient advocates, and SMEs.

For each country, after a thorough context analysis, a stakeholder list will be created, defining their level of involvement, aligning them with the Action scheme, managing expectations, and assessing their interest and support. Ongoing works tracking will keep everyone informed, saving time. Building strong relationships with stakeholders will be a priority to drive shared and impactful actions, bridging the gap between evidence and clinical practice.

All stakeholders will be involved from the outset and throughout network activities, with tailored engagement approaches based on their professional profiles.

- **HPs** involved in cancer prevention: objectives include providing training opportunities, knowledge exchange, capacity building, and career development for future cancer prevention scaling. HPs' representatives will be early participants in Medi-CaSE strategic planning.
- **Policymakers:** regular updates through reports, articles, and newsletters will facilitate knowledge-sharing and effective cancer control initiatives. In-person or virtual meetings will offer direct discussions on relevant topics.
- **General scientific community:** dissemination of Medi-CaSE outputs through publications, participation in seminars, and conferences hosted by third parties.
- **Community and religious leaders:** leveraging faith communities and networks for multi-dimensional interventions. They will be involved in COST Action activities to ensure support, dialogue, and training.
- **Local NGOs and patients' advocates:** essential for data collection, evidence building, tailoring activities to local needs, and overcoming socio-cultural barriers. They will raise cancer awareness and influence target population attitudes and behaviors.
- **Small and Medium Enterprises (SMEs):** collaborative relationships with SMEs to advance cancer early detection with new screening tests and technologies, improving cancer outcomes. Collaboration in the areas of cancer early detection will be pursued to have access to relevant equipment and technologies and to make it available for the network.
- **Community-based non-governmental organizations:** early involvement to mobilize resources and promote policies responsive to community needs.

In summary, the plan focuses on engaging a diverse range of stakeholders to enhance cancer prevention and early detection, promoting evidence-based actions and innovative approaches.

3. IMPACT

3.1. IMPACT TO SCIENCE, SOCIETY AND COMPETITIVENESS, AND POTENTIAL FOR INNOVATION/BREAKTHROUGHS

3.1.1. SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

Medi-CaSE, through its networking activities in Mediterranean and other countries as well, and based on Mediterranean paradigm, has the potential to significantly improve the health and quality of life for both men and women.

It will have a **scientific impact** by sharing certified knowledge and evidence-based practices in cancer prevention, fostering individual professional growth, and enhancing a collaborative approach to cancer control. The diversity of experiences within the network will encourage research and innovation in cancer prevention.

Practically, scientific achievements will be disseminated through training opportunities, including online and in-person events, and ad-hoc training initiatives. These efforts will enhance data collection and interpretation for cross-country comparisons. Additionally, Medi-CaSE will facilitate common research projects, especially for countries with limited funding opportunities, aiming to access international funding.

Innovation impact will be realized through open-access publications, guidelines, and consensus statements, reaching a wide audience, including the scientific community, HPs, researchers, and other key stakeholders. The technological impact will focus on discussing innovative screening tests and approaches during Medi-CaSE meetings and workshops. It aims to address shared research questions, provide guidance on new technologies, explore self-sampling modalities for CC screening, and investigate the use of Artificial Intelligence in BC screening. Medi-CaSE will also explore personalized screening protocols based on individual characteristics, making guidance available in this complex field. Additionally, it will consider the use of interactive modalities and social media to increase

awareness and participation in cancer screening.

The **socio-economic** impact will benefit the general population by promoting cancer awareness and screening access. The Action will provide guidance on planning awareness initiatives, especially for vulnerable populations, and work to reduce health inequalities and access barriers. The involvement of stakeholders will enhance the initiative's impact and contribute to overcoming socio-economic and cultural obstacles, ultimately increasing cancer screening participation and access equity.

In summary, the following impacts can be highlighted, differentiated based on alternative time-horizons.

Short-term impact

- Development of a joint multidisciplinary international network for enhancing cancer screening across the Mediterranean countries.
- Elaboration of shared scientific evidence, adopting different methodologies (e.g. scoping review, consensus conference, etc.).
- Dissemination of knowledge and evidence among both the scientific community and the general population.
- Creation of a common research platform for identifying interesting research questions in cancer screening, defining future study protocols and exploring new funding opportunities.
- Promoting inclusiveness and gender balance in the framework of Medi-CaSE.
- Fostering knowledge and skills enhancement among local HPs through multiple training opportunities, for promoting the straightforward adoption of evidence-based protocols and good practices into clinical routine.

Long-term impact

- Draft of guiding documents on cancer screening for HPs, screening managers, and policymakers.
- Improving awareness and knowledge regarding cancer screening in local HPs, policymakers as well as in the general population.
- Definition of common actions for facing the main emerging barriers in screening participation with a specific focus on hard-to-reach groups.
- Facilitating the assessment and adoption of new technologies in cancer screening, additionally investigating the potential economic costs.
- Favoring the adoption of evidence-based and best practices in cancer screening programs across the Mediterranean area.
- Evaluation of the short- and long-term effects in the framework of the Action, considering the potential impact on the local policies as well as on the clinical practice.
- Improving health and quality of life of several men and women eligible to different cancer screening protocols (i.e. BC, CC, and CRC).

3.2. MEASURES TO MAXIMISE IMPACT

3.2.1. KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

Knowledge creation. Medi-CaSE aims to improve understanding in cancer prevention across the Mediterranean area and other COST countries, providing a complete and updated state-of-art of local situations, highlighting (and if possible bridging) gaps in current knowledge, and providing joint solutions for enhancing cancer control. The multidisciplinary nature of the network will enhance the creation and dissemination of comprehensive knowledge through scientific publications, and these outputs will be made easily accessible to researchers, HPs, stakeholders, and policymakers.

Medi-CaSE intends to raise awareness regarding cancer prevention and control among relevant stakeholders. In this regard, policymakers will benefit from the provision of a clear guidance aimed at facilitating transferability of best-practices in routines and on a larger scale, exploiting local commonalities (both geographical and socio-cultural).

Knowledge creation will take advantage of a cascade process that starts from Medi-CaSE members and will have a direct impact to local levels through the enabled commitment of national representatives. Finally, Medi-CaSE can promote common projects on cancer screening for answering the more pressing research questions in the field.

Knowledge transfer. Training initiatives in cancer prevention (with specific focus on BC, CC, and CRC control) represent a priority of Medi-CaSE, and constitute the key instrument for knowledge transfer.

The definition of the training schedules will be preceded by in-depth discussions, to adopt shared solutions for enhancing knowledge and skills. Training will be as far as possible devoted to multidisciplinary activities, involving all the profiles engaged in cancer prevention (e.g. physicians, epidemiologists, technicians, laboratory staff, midwives, programme and data managers, etc.) to reach maximal participation and outcomes. These opportunities will include: Training Schools (TS), STMS,

workshops, and virtual mobility opportunities as webinars, providing a fast-track access for young researchers. Indeed, a fixed number of places will be reserved to young researchers.

In the framework of the Action, decision-makers will receive the necessary guidance for developing medium- and long-term national strategies and roadmaps to promote the sustainability and effectiveness of cancer prevention programs, and their reproducibility in similar contexts.

The results dissemination to the entire scientific community and public opinion will be ensured through reports, peer-reviewed publications, and documents for lay people. These publications will prefer (as possible) an open access option for increasing accessibility to all interested users. Moreover, these deliverables will be spread through web-portals and social media. Finally, results from scientific publications will be employed to produce informative materials for the general public and stakeholders.

Career development. Medi-CaSE will focus on involvement as much as possible Young Researchers and Innovators (YRI), from a wide range of different countries and professional backgrounds. The promotion of young career opportunities will be a core of Medi-CaSE activities, promoting mobility opportunities in cancer prevention, and encouraging cross-countries projects, and training courses. In this context, Medi-CaSE will facilitate the involvement and the exchanges between junior and senior members, providing relevant benefits to all, endorsing insights on cancer prevention moving beyond geographical and disciplinary frontiers. Considering career opportunities, Medi-CaSE will promote collaborative research groups supporting them in grant applications, specifically encouraging younger members to be actively involved. Boosting young researchers' careers will go hand-in-hand with fostering the inclusiveness (comprising a major involvement of ITCs), and the gender balance, considering Medi-CaSE composition and its activities.

3.2.2. PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

In alignment with Medi-CaSE objectives, the main communication goals are:

- Higher level of awareness among the general public on the importance of cancer secondary prevention, with a specific focus on BC, CC and CRC;
- Higher level of information among HPs, policy-makers and the general public on opportunities for BC, CC, and CRC early diagnosis and screening;
- More favorable policies in relation to cancer prevention, early diagnosis and screening;
- Enhanced media's attention as regards the Action;
- Spotlight on the added value arising from EU's commitment and role of the COST Action in promoting health and societal progress in the Mediterranean area.

Medi-CaSE aims to spread a culture of health promotion and cancer secondary prevention throughout the Mediterranean, especially in countries with more initial cancer control policies and towards hard-to-reach groups (e.g. migrants, rural population, people with disabilities). For them, increasing cancer prevention awareness is particularly important as prejudices and false beliefs need to be mitigated, while conducive attitudes require further impulse.

Thus, particular efforts will be dedicated to vulnerable groups and women (considering the relevant burden of BC and CC). The selection of target sub-groups to be addressed through tailored communication initiatives will be performed by workshop(s) at network and local level.

Co-operation with advocacy/charity groups/NGOs active on ground is crucial for understanding the cultural dimensions of attitudes, beliefs and knowledge about cancer. Such actors will represent both target audience and active members within Medi-CaSE communication strategy. They have the potential to act as influencers and are able to offer channels to reach lay and/or disadvantaged people in community settings. For these reasons, they will be identified and informed through tailored communication materials/means and involved in the communication planning, through workshops and/or meetings. Dialogue initiatives towards community and religious leaders will be launched for the same reasons.

To identify the subjects to be involved, workshops and/or webinars among members will be organized, using shared matrices for mapping and describing relevant actors in each country.

Media will be addressed as crucial gateways for spreading information, raising awareness and changing culture and attitudes. Information will be delivered periodically through press releases. In particular, at launch and end of the Action a press event will be organized.

A Medi-CaSE website will be developed to meet several dissemination objectives and give the opportunity to reach diverse audiences, as well as to spread messages at different levels of complexity. More specifically, Medi-CaSE website will allow to:

- Make available up-to-date information for lay people on how to prevent cancer;
- Host multiple communication/educational tools like videos, stories, printable materials, blogs etc.

Link to other resources that may offer contents in line with the Action scope and reinforce the informative value of the initiatives;

- Offer reserved areas for Medi-CaSE members and stakeholders, to access to *ad-hoc* information/materials and take part in specific activities as e-learning modules and/or virtual networking initiatives;
- Make available the Action's outputs (open-source databases, open access journal articles, guidelines, toolkits, etc...).

In parallel, a communication campaign will be developed and declined by country-specific needs, in order to raise awareness on the importance of cancer prevention. This campaign will be multi-target and multi-channel for maximizing its impact and will be co-created with relevant stakeholders.

Communication will be also organized via various social media channels established by the Action and COST Association, for spreading messages to lay people and scientific community, and for multiplying communication activities in general. The opportunity to have Action-specific social media accounts will be discussed within the "Communication and Dissemination" Working Group 6 (WG)).

At the beginning of the Action, the communication strategic plan will be defined through a dedicated workshop within WG6, involving partners and, possibly, external experts. This dissemination strategy will be discussed and shared at the start of the Action for defining the main contents to be disseminated, the general outlines, the major target groups, and the adequate communication means. Further operational plans will be prepared every year, and regularly updated.

The Medi-CaSE dissemination plan will be defined, including the publication list and delivery timing ("publication plan") as well as a planning for participation in conferences (including third parties' meetings). Papers for peer-reviewed journals will be open access and archived into a common repository. A final dissemination conference will be organized.

Through its communication activities, Medi-CaSE aims to support the building and/or strengthening of an international "*community for beating cancer*". The existing relationships among the involved countries will be intensified while new connections will be implemented, ensuring fruitful debates on local experiences. Moreover, further collaborations with other countries (even external to the Mediterranean area) will be crucial for enhancing reproducibility, and supporting the definition of accepted recommendations.

Concerning exploitation, Medi-CaSE outputs will be available free-of-charge (e.g. context-specific guidelines, toolkits, repositories, etc.).

4. IMPLEMENTATION

4.1. COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

4.1.1. DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

For an effective and updated networking, at least one annual (preferably in-person) meeting, held alternately in different Medi-CaSE member countries, will be held. These initiatives, addressed to all members, will foster the promotion and dissemination of Medi-CaSE activities, and the exchange of updated information, discussing current upgrades in cancer secondary prevention. If appropriate, policymakers and stakeholders will be invited to join the entire meetings or specific sessions.

The following WGs will be formed to handle different priorities emerging from the analyses of the current scenario of cancer prevention in the Mediterranean area:

- **WG1:** cancer early diagnosis and screening implementation, optimization, data collection, and monitoring;
- **WG2:** research platform in cancer screening across the Mediterranean;
- **WG3:** training of professionals and stakeholders in cancer secondary prevention;
- **WG4:** finding the best approaches for increasing the participation of the eligible population in cancer early diagnosis/screening programs, with a focus on vulnerable and hard-to-reach groups;
- **WG5:** integration of cancer secondary prevention within ongoing health services;
- **WG6:** dissemination and communication.

WG1: cancer early diagnosis and screening implementation, optimization, data collection, and monitoring;

This WG aims to define a set of context-adapted priorities in cancer secondary prevention, enhancing current activities across the Mediterranean, simultaneously implementing (or adapting) a systematic monitoring to support quality improvement. The essential requirements of early diagnosis as well as of more structured screening policies will be described, with special attention to sustainability. Moreover, this WG will be the opportunity to review common criticalities and propose joint solutions.

T1.1: Priority analysis. T1.1 aims to provide a priority list and a set of minimum requirements useful for implementing and monitoring early diagnosis and cancer screening programs (BC, CC and CRC), underlining the elements needed for an effective and sustainable implementation of these two approaches. This list will be based on available evidence in the field.

T1.2: Best experiences and evidence-based practices. This task aims to gather the virtuous and successful experiences in cancer secondary prevention within Medi-CaSE, to provide models to be applied in similar contexts. Evidence-based guidelines will be collected, by fixing a gold-standard with which to strive, and they will be spread through a common communication platform. Then, Medi-CaSE will offer guidance to the local adaptation processes.

T1.3: Context analysis of information systems (IT). Semi-structured surveys will be administered to country representatives for defining the features of the IT systems in use and for identifying room for improvement. Review of data protection regulations, and of their requirements with respect to IT systems design and to the development of monitoring initiatives will be explored.

T1.4: Essential monitoring indicators. Through periodic brainstorming as well as literature review, a list of *must-have* indicators for early diagnosis and screening monitoring will be established for cross-countries benchmarking.

T1.5: Data collection training. Within Medi-CaSE, in collaboration with WG3, training initiatives for data collection and interpretation will be arranged, addressed to policymakers, data managers and HPs.

T1.6 Sustainability and cost-effectiveness. Sustainability and cost-effectiveness of different cancer prevention policies by context will be discussed. In particular, ongoing or past experiences in cancer prevention economic assessments will be retrieved to consider the most suitable methodologies to be adopted and how to face emerging criticalities. T1.6 aims to produce a position paper on current methodological perspectives and design a common framework for guiding local assessments. Furthermore, regarding affordability, the procurement of equipment and technologies will be facilitated discussing the viability of common regional funds for ensuring access to high-quality products at the lowest price, notwithstanding country's size or economy. For countries with small-scale markets, these mechanisms could ease access to tests, consumables, and drugs. Community-based non-governmental organizations will be involved.

T1.7: Cancer prevention scaling-up. This task aims to debate the potentialities of scaling-up cancer prevention services, proposing country-specific road-maps to accelerate the implementation of effective programs.

WG2: Research platform in cancer screening across the Mediterranean

This WG aims to identify common research questions in the cancer prevention framework, for elaborating prospective and retrospective research protocols for cross-countries investigations. WG2 aims to promote the elaboration of a common research agenda, adopting a multidisciplinary approach and sharing international funding opportunities. The active participation of ITCs will be boosted throughout the process. Measurable outputs of this WP will include joint publications and grant submissions.

T2.1: Research topics. Medi-CaSE will give the opportunity for discussing and defining challenging research topics in cancer secondary prevention (e.g. new tests, innovative screening algorithms, etc.). In particular, a state of play of existing projects will be defined considering key research questions (e.g. screening personalization, technological advancements in cancer screening, etc.). This preliminary analysis will be valuable for defining new research protocols, taking into account feasibility.

T2.2: Screening personalization. This task aims to assess the most updated strategies for risk stratification in cancer secondary prevention. In particular, the potential impact of similar tools in systems with more structured cancer screening programs will be explored, underlining common research areas and the potential communication challenges. Ongoing projects among members will be retrieved, for disclosing insights on clinical methodologies, research protocols and emerging issues/solutions. Concurrently, the potential impact of a similar process in LMICs will be investigated, exploring the potential challenges in resource-constrained settings.

T2.3: Genetic predisposition and cancer secondary prevention. This task aims to gather best-practice from Medi-CaSE members on cancer genetic predisposition management for producing common recommendations to be applied in different contexts. This task will identify the different classifications applied as well as the screening protocols adopted for providing a comprehensive overview of the topic, especially considering inputs from experts in the field. Moreover, the potential translation of comparable services in LMICs will be considered.

T2.4: Technological Innovation. The impact of new technologies in cancer early diagnosis and screening will be debated. Particular attention will be directed to Artificial Intelligence, collecting ongoing and past projects in this field, for sharing methodologies, criticalities, advancements, etc. Moreover, the use of new tests especially for CC (e.g. self-sampling approaches) and for the subsequent triage of positive

women will be assessed, considering also the feasibility of a similar approach in case of constrained resources. Evidence will be gathered through a scoping review on multiple scientific databases, while feasibility will be investigated through the inputs of network members and key stakeholders. T2.4 will allow to identify potential gaps in current knowledge, by pinpointing interesting questions to be tackled by the Network.

T2.5: Protocols for new studies. Gaps in existing knowledge will be addressed drafting common protocols, involving multiple countries, to be presented for funding demands.

WG3: training of professionals and stakeholders in cancer secondary prevention.

This WG aims to provide training for professionals and stakeholders already or potentially involved in cancer secondary prevention, to increase their knowledge and skills and to implement best and evidence-based practices. In particular, specific initiatives will be arranged considering BC, CC and CRC for sharing evidence-based processes (including the data collection and analysis as specified in WG1), and current innovations in these fields. All efforts will be characterized by a multidisciplinary approach, joining different professional profiles for ensuring a comprehensive screening assessment. All venues will promote the involvement of young participants and women.

T3.1 - Training needs assessments. A preliminary survey of formative needs will be conducted among members to identify the areas more requiring formative interventions.

T3.2 Planning and implementing the training courses. A time-frame of formative opportunities will be defined, including different modalities (as TS, virtual mobility opportunities and STMS) for exploiting at best the events' magnitude (in terms of participation and practical implications). Main topics will be: BC, CRC and CC early diagnosis, screening and treatment. The participation of local operators involved at different levels in BC, CRC and CC prevention will be promoted, by fostering multidisciplinary participation. These opportunities aim to adopt a cascade approach, for maximizing the effects even for professionals not directly participating in them. During TS a special attention will be given to new research topics for creating specific WGs.

This task aims to organize:

- a TS for 20-30 attendees, favoring multidisciplinary participation.
- Symposium at least one international conference for promoting the Action and its results.
- Annual workshops (in person or online) in which partners can meet and discuss the results of their collaborations
- STMs of 1-4 weeks to perform small projects to train members and advance the WGs goals.

T3.3: Periodic refreshing. Regular updates, mainly using online modules, will be ensured throughout the Action. All educational materials will be shared among courses' participants and Medi-CaSE members using the reserved area of Medi-CaSE website and/or periodic newsletters.

T3.4: Evaluation and Monitoring. The evaluation of training, in terms of knowledge acquisition and participants' satisfaction, will be carried out, using pre-/post- questionnaires.

WG4: finding the best approaches for increasing the participation of the eligible population in cancer early diagnosis/screening programs, with a focus on vulnerable groups

This WG aims to discuss common and effective strategies for increasing the general population awareness and participation in BC, CC, and CRC early diagnosis and screening programs, providing guidance to Medi-CaSE members. The WG will additionally focus on activities addressed to hard-to-reach groups (e.g. migrants, people from deprived areas, habitants of rural areas, people with disabilities), defining actions mainly addressed on socio-cultural characteristics of these groups and/or for increasing service accessibility.

T4.1 – Collecting evidence on cancer prevention awareness and cancer screening invitation strategies.

This task aims to retrieve effective awareness approaches, and invitations strategies to cancer screening, with a specific focus on hard-to-reach populations. Besides, the potential role of new technologies in this field will be explored. This review will identify main vulnerable groups (with a lower participation to screening), and the more effective strategies for involving them.

T4.2 - Context analyses. *Ad-hoc* context analyses will be carried out among Medi-CaSE members for describing the methods already in use for inviting the target population to cancer secondary prevention services, with a more in-depth focus on the use of innovative technologies for promoting participation. Besides providing a complete local framework, this task aims to retrieve best practices potentially acting as role models for other contexts.

T4.3 - Map of vulnerable populations. Through discussions and meetings, a map of these disadvantaged groups will be built for each setting, defining a priority agenda of groups to be targeted in *ad-hoc* cancer prevention approaches. Awareness initiatives and campaigns targeted to these groups will be gathered, for providing an overall picture and finding best practices to be potentially applied in other contexts, taking advantage of the geographical and socio-cultural commonalities.

T4.4 – Future cross-countries research insights. This task will be devoted to exploring the likelihood of planning cross-countries experiences for testing and evaluating innovative awareness or recruitment approaches in selected settings. Medi-CaSE members will provide methodology technical support, and the opportunities of new collaborations will be explored.

WG5: integration of cancer secondary prevention within ongoing health services

This WG aims to debate the feasibility and effectiveness of specific interventions of integration of cancer secondary prevention initiatives within ongoing health services.

T5.1: Collecting evidence on cancer secondary prevention integration experiences. This task aims to collect information on existing integration projects, summarizing organizational inputs and outcomes.

T5.2: Context analyses. Current existing experiences in different Mediterranean countries will be collected, compared and discussed, leading to the definition of best practices to be followed and shared recommendations for effective implementation.

T5.3: Guidance to policymakers and stakeholders. The results of T5.1 and T5.2 will be exploited for drafting and disseminating a guideline addressed to policymakers and stakeholders.

WG6: dissemination and communication.

The main aims are:

- Gaining the support from key-stakeholders;
- Spreading information on Medi-CaSE and its activities among the scientific community and the general population (targeting messages and channels by the public features);
- Influencing public health decisions;
- Raising attention on the COST Action added value.

This WG will act in close coordination with all other WGs, to effectively spread Medi-CaSE activities and outputs.

T6.1 – Communication management. This task includes: WG coordination and meetings organization; design and implementation of the Action's communication plan; definition and development of communication materials; promotion of an active cooperation regarding communication activities with community stakeholders.

T6.2 – Website development and update. This task aims to develop the Medi-CaSE website for spreading information on its activities to the actual/potential members and to the general population. The website will be regularly updated, and potentially maintained after the formal end of the Action. This tool will offer a reserved area to members for accessing additional materials.

T6.3 – Stakeholders engagement. This task includes multiple sequential activities, as: the initial mapping of local relevant stakeholders (including advocacy groups, NGOs and citizens' associations), the implementation of stakeholders' consultations, the promotion of a linkage of stakeholders within Medi-CaSE, the gain of inputs to inform the strategic planning, and the continuous nurturing of these relationships throughout the entire Action's timeline (e.g. meetings, newsletters, posts).

T5.4 – Media relations. This task includes: drawing up media accounts' lists, preparation of press packages, organization of media events, and coordinating and monitoring media communication.

T5.5 – Outputs dissemination. This task includes: drawing up the publication plan, planning and preparing participation in conferences, knowledge brokering documents/tools and the final scientific meeting to disseminate the Action achievements (in cooperation with other involved WGs).

4.1.2. DESCRIPTION OF DELIVERABLES AND TIMEFRAME

WG1: cancer early diagnosis and screening implementation, optimization, data collection, and monitoring;

D1.1 Priority assessment report and checklist of the minimum requirements for implementing effective services for BC, CC and CRC early diagnosis and screening (M9).

D1.2 Collection of best practices, guidelines and adaptation to local demands (M11).

D1.3 IT systems' report (M16).

D1.4 List of essential indicators for cancer early diagnosis and screening monitoring (M18).

D1.5 Agenda for training on data collection (M20).

D1.6 List of ongoing or past experiences on cost-effectiveness assessments (M18).

D1.7 Countries' road-maps for scaling-up cancer prevention policies (M24).

WG2: Research platform in cancer screening across the Mediterranean

D2.1 Report on identified research topics (M38).

D2.2 Report on current risk stratification approaches (M41).

D2.3 Report on genetic predisposition management in cancer secondary prevention (M44).

D2.4 Report on existing Artificial Intelligence experiences (M44).

D2.5 Research protocols

WG3: training of professionals and stakeholders on cancer secondary prevention

D3.1 Learning needs research report (M12).

D3.2 Training programme and materials (M17, M23, M29, M35, M41) to be used for training refreshment.

D3.3 Yearly report on courses implemented (M24, M36, M48).

WG4: finding the best approaches for increasing the participation of the eligible population in cancer early diagnosis/screening programs, with a focus on vulnerable groups

D4.1 Scoping literature review on cancer awareness and screening invitation strategies (M26).

D4.2 Context analysis report (M31).

D4.3 Country-based maps of vulnerable population groups and interventions to reach them (M33).

D4.4 Report on identified research topics (M46).

WG5: integration of cancer secondary prevention within ongoing health services

D5.1 Review report (M38).

D5.2 Country-based report on integration initiatives (M40).

D5.3 Guideline document for policymakers and stakeholders (M43).

WG6: Dissemination and communication

D6.1 Communication Plan (M6).

D6.2 Website release (M12).

D6.3 Stakeholders map and involvement plan (M4).

D6.4 Communication package (M10). Press packages at launch and end of the Action (M12, M46).

D6.5 Dissemination Plan (M11).

4.1.3. RISK ANALYSIS AND CONTINGENCY PLANS

| Risk (high, medium, low) | Contingency Actions |
|---|--|
| Suboptimal Network size at the beginning of the Action (Low) | From the beginning of the Action, several Mediterranean countries and other COST members will be represented. The network is already consistent, gathering several ongoing fruitful collaborations. To ensure further geographical representation, the future Medi-CaSE expansion through dissemination activities (WG6) and personal contacts (by all members) will be put in place. In particular, new representatives from Mediterranean and other countries not yet included will be identified making contacts with local Ministries of Health and International Organizations. The inclusion of new members from countries already involved in Medi-CaSE will be encouraged, favoring the multidisciplinary approach to cancer prevention. |
| Reluctance and/or practical difficulties in involving relevant stakeholders across the Mediterranean within Medi-CaSE and its activities. (Medium) | Information and shared decision-making initiatives for involving key stakeholders during the whole Action's implementation will be carried out. Their continuous involvement will be a core activity of WG6. Their preliminary mapping and the following definition of a " <i>Stakeholder engagement plan</i> " will be valuable for containing this risk. Besides these specific actions, the active involvement of key stakeholders will be part of all WGs, as it is a prerequisite for the success of Medi-CaSE. Medi-CaSE members already present a strong engagement with multiple local key-stakeholders. |
| Difficulties in involving the general population and hard to reach subgroups. (Medium) | The participation of local public institutions from different Mediterranean countries in Medi-CaSE is a sign of commitment. Moreover, the active involvement of local advocacy groups, NGOs and citizens' associations as part of the workflow aims to boost general involvement. The use of multiple communication means (e.g. traditional and new media) for enhancing these activities represent an added value (see WG6). |
| Difficulties in data collection within the involved countries for technical difficulties and limited professionals training. (Medium) | Sharing a list of essential indicators for cancer prevention evaluation is a specific task of WG1. This activity will be preceded by careful context analyses, assessing the local IT characteristics, to propose feasible tools focusing on common data easily retrieved among different databases. Moreover, for limiting this risk, specific training will be performed within Medi-CaSE regarding data entering, analysis, and interpretation, addressed to HPs, and programme and data managers. All data will be retrieved and stored in agreement with EU General Data Protection Regulation. |
| Low medium and long-term political commitment and financial sustainability. (Medium) | The strong commitment of involved Governments to deal with Non Communicable Diseases and to introduce cancer control interventions, may propel the identification of additional resources to overcome financial constraints. The strengthening of an international network as Medi-CaSE may facilitate the identification of additional financial resources. The effects on cancer burden are long-term, but those on health systems can early be seen, encouraging policymakers to additional capital expenditures. Attention to sustainability and cost-effectiveness will be part of WG1. |
| Difficulties to sensitize local professionals and policymakers to cancer prevention, to equity of care, and gender-related issues. (Low) | Communication, training and capacity building activities as stated in the Action are multiple and all marked by an equity oriented approach. The identification and engagement of local key actors will start early, and their engagement will be promoted by the use of multiple means (e.g. policy dialogues, newsletters, publications, etc.). For improving involvement, COST website as well as Medi-CaSE website will be used. Moreover, additional campaigns will be performed on social media. |

| | |
|---|---|
| Limited participation of professionals to proposed training initiatives (Low) | Multidisciplinary participation in training courses will be favored, involving all profiles engaged at different levels in cancer secondary prevention and care. For increasing participation, online modules will be performed, and all formative materials will be released through the Medi-CaSE website. Formative initiatives will be additionally promoted on the COST website. Moreover, additional information will be disseminated through periodic newsletters and presentations to conferences hosted by third parties. To increase specialists' participation, the implementation of connections with professional organizations and scientific societies will be considered. WG3 will be devoted to training, offering different educational opportunities and periodic updates. |
| Sustainability of the network in terms of members' turnover (Medium) | This risk will be contained by actively engaging a large enough number of members for each WG. Moreover, from initial phases, the participation of professionals from different organizations and countries will be fostered, and in case of turnover, an effective handover will be promoted. |
| Punctual delivery (Low) | All members will be committed for assuring the punctual achievement of all deliverables and tasks. The Action Chair and the Management Committee will be in charge of coordinating the Action and its members' endeavors. Deadlines and timesheets will be established with sufficient advance and reminders will periodically be sent. Emerging difficulties will be discussed among the entire Network for finding alternative options. |
| Low involvement of young researchers and/or students (Medium) | The importance and focus on YRIs involvement will be expressly stated in the Action agenda, highlighting the importance of mentorship and career development. For all the training opportunities, a fast-track access modality for young professionals will be implemented, setting a fixed number of reserved places. |

4.1.4. GANTT DIAGRAM

| Activity | Year 1 | | | | Year 2 | | | | Year 3 | | | | Year 4 | | | |
|--|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
| | Q 1 | Q 2 | Q 3 | Q 4 | Q 1 | Q 2 | Q 3 | Q 4 | Q 1 | Q 2 | Q 3 | Q 4 | Q 1 | Q 2 | Q 3 | Q 4 |
| Launch of Medi-CaSE and WG leader definition | ■ | | | | | | | | | | | | | | | |
| Kick-off meeting | ■ | | | | | | | | | | | | | | | |
| Regular online meetings | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| Workshops | | | | ■ | | | | ■ | | | | ■ | | | | ■ |
| Training schools | | | ■ | | ■ | | ■ | | | ■ | | ■ | | ■ | | |
| Virtual mobility opportunities | | | | | ■ | ■ | | | | | ■ | | | ■ | | |
| STMS* activities | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| Website launch and updates | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| WG1-6 activities and deliverables | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |

REFERENCES

- [1] Sung H, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021 May;71(3):209-249.
- [2] Fidler MM, et al. The global cancer burden and human development: A review. *Scand J Public Health.* 2018 Feb;46(1):27-36.
- [3] <https://gco.iarc.fr/>
- [4] Kulhánová I, et al. Profile of cancer in the Eastern Mediterranean region: The need for action. *Cancer Epidemiol.* 2017 Apr;47:125-132.
- [5] Belkacémi Y, et al. Fight against cancer around the Mediterranean area: "Many hands make light work!". *Crit Rev Oncol Hematol.* 2012 Dec;84 Suppl 1:e1-5.
- [6] Jelenc M, et al. Developments in National Cancer Control Programmes in Europe - Results From the Analysis of a Pan-European Survey. *Cancer Control.* 2021 Jan-Dec;28:10732748211041508.
- [7] <https://www.iemed.org/publication/migrations-in-the-mediterranean-region/>
- [8] Mentella MC, et al. Cancer and Mediterranean Diet: A Review. *Nutrients.* 2019 Sep 2;11(9):2059.
- [9] <https://www.who.int/publications/i/item/9789240014107>
- [10] <https://www.who.int/europe/news-room/fact-sheets/item/cancer-screening-and-early-detection-of-cancer>
- [11] <https://apps.who.int/iris/handle/10665/351396>
- [12] Schünemann HJ, et al. European Commission Initiative on Breast Cancer (ECIBC) Contributor Group. Breast Cancer Screening and Diagnosis: A Synopsis of the European Breast Guidelines. *Ann Intern Med.* 2020 Jan 7;172(1):46-56.
- [12] <https://apps.who.int/gho/data/view.main.UHCCERVICALCANCER>
- [13] Giordano L, et al. The EUROMED CANCER network: state-of-art of cancer screening programmes in non-EU Mediterranean countries. *Eur J Public Health.* 2016;26(1):83-89.
- [14] Islam RM, et al. Barriers to Cervical Cancer and Breast Cancer Screening Uptake in Low-Income and Middle-Income Countries: A Systematic Review. *Asian Pac J Cancer Prev.* 2017; 18(7): 1751–1763.
- [15] <https://www.who.int/publications/i/item/9789240014107>
- [16] <https://www.who.int/initiatives/global-breast-cancer-initiative>
- [17] <https://www.who.int/publications/i/item/9789241506236>
- [18] <https://apps.who.int/iris/handle/10665/342366>
- [19] <https://apps.who.int/iris/handle/10665/119811>
- [20] Olayemi E, et al. Guidelines in lower-middle income countries. *Br J Haematol.* 2017 Jun;177(6):846-854.
- [21] Farazi PA, et al. Awareness of human papilloma virus and cervical cancer prevention among Greek female healthcare workers. *Eur J Cancer Prev.* 2017 Jul;26(4):330-335.
- [22] Shieh Y, et al. Population-based screening for cancer: hope and hype. *Nat Rev Clin Oncol.* 2016

Sep;13(9):550-65. doi: 10.1038/nrclinonc.2016.50. Epub 2016 Apr 13.

[23] Jarm, K, et al. Quality assured implementation of the Slovenian breast cancer screening programme. PloS one. 2021, vol. 16, no. 10, str. [1-16].

[24] https://ec.europa.eu/commission/presscorner/detail/en/ip_22_702

[25] <https://www.consilium.europa.eu/en/press/press-releases/2022/12/09/council-updates-its-recommendation-to-screen-for-cancer/>