Towards large-scale adaption and tailored implementation of evidence-based primary cancer prevention programmes in Europe and beyond (PIECES)

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Executive Summary

Deliverable D8.8 outlines the initial joint work plan for scientific collaboration in the 'Prevention and Early Detection Cancer' cluster. It sets out the pathway followed for the associated projects funded under the Mission Cancer framework to achieve the target of Mission as set by the EC. As stated in the topic description it is a collective effort agreed upon with all project coordinators in the cluster. The document begins by introducing the Mission Cancer program and the projects involved in the cluster. It then details how these projects are currently structured to synergize their work and share best practices in research and innovation areas. A plan has been developed and discussed for future steps, emphasizing greater involvement of project partners in joint working groups to amplify collective efforts. Also, the possibility of enhancing collaborative impact with other cancer clusters through joint policy recommendations will be explored. Success of the cluster hinges on active participation from project partners and coordinators, supported by the European Health and Digital Executive Agency (HaDEA).

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Abbreviations & Acronyms

AI	Artificial Intelligence
AR	Augmentin Reality
EASO	The European Association for the Study of Obesity
EC	European Commission
EHMA	European Health Management Association
CPE	Cancer Patients Europe
CPW	Cancer Prevention at Work: Occupational health surveillance in the implementation of prevention of infection-related cancer
CO-CAPTAIN	Cancer prevention among individuals with mental ill-health: co-adapting and implementing patient navigation for primary cancer prevention
DMP	Data Management Plan
GA	Grant Agreement
HCV	*Hepatitis C virus*
Hp	*Helicobacter pylori*
HPV	*Human Papillomavirus*
LL	Living Labs
NKUA	National & Kapodistrian University of Athens
ONCODIR	Evidence-based Participatory Decision Making for Cancer Prevention through implementation research
4P-CAN	Personalized CANcer Primary Prevention research through Citizen Participation and digitally enabled social innovation
PIECES	Towards large-scale adaptation and tailored implementation evidence-based primary cancer prevention programmes in Europe and beyond
PREVENT	Improving and upscaling primary prevention of cancer by addressing childhood obesity through implementation research – the PREVENT approach
R&I	Research & Innovation
QoL	Quality of Life

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1. Introduction

Purpose of the Deliverable

This deliverable sets out to establish a preliminary plan for the projects within the "Prevention and early detection" cluster of the Mission Cancer initiative. Its goal is to coordinate and integrate the collective endeavors of these projects, fostering an environment where activities can mutually benefit from each other. This collaborative approach is intended to amplify the overall impact, contributing significantly to the Mission Cancer's aspirational objective of enhancing the lives of over 3 million individuals by 2030. The projects are responsible to provide shared strategies to help reduce disparities in care and enhance access to healthcare services. The cluster's efforts will be coordinated by engaging in various joint activities, beginning with the formulation of a unified work plan for Research and Innovation, Citizen engagement, Addressing inequalities, Common chapter in DMP, Cluster video or/and brochure. This deliverable presents an initial collective work plan for all the projects, aiming to underscore the commonalities and methodologies that can be further enriched through this collaborative effort.

Structure of the Deliverable

Initially the widespread impact of cancer and sets forth the ambitious goals of the Mission is provided. The document then details the individual projects within the cluster, each targeting different facets of cancer prevention and treatment. Co-CAPTAIN, CPW, ONCODIR, PIECES, 4P-CAN and PREVENT address unique challenges in cancer prevention, ranging from mental health to occupational health surveillance and integrate primary prevention programs into existing systems, highlighting their diverse methodologies and target populations. Further, the document provides a matrix of scientific cross-cutting domains between all sister projects such as:

- Research & Innovation strategies
- Health policy
- Social & Behavioural Sciences
- Technology & Digital Health Solutions
- Community engagement & participatory research

Discussion for the development of a 'knowledge map' to integrate and leverage the diverse inputs from projects. Finally, the document concludes with a reflection on the work plan's dynamic nature and the importance of future cluster meetings for refining strategies and enhancing collaboration. This structure ensures a holistic approach towards achieving the objectives of the Mission Cancer and improving the quality of life for EU citizens.

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2. The Cluster for the Mission Cancer

2.1. What is Mission Cancer

Cancer indiscriminately impacts individuals of all ages, genders, and social standings, posing a significant challenge to patients, their families, and societies. Data from the European Cancer Information System reveals that annually, 2.7 million individuals in Europe are diagnosed with cancer, and 1.3 million succumb to this illness. Without proactive measures, the number of new cancer cases is projected to rise to over 3.24 million by 2040. To counter these alarming trends, the Cancer Mission has set forth ambitious and clear goals. Through collaborative efforts involving citizens, stakeholders, and Member States across Europe, the Mission on Cancer, in conjunction with Europe's Beating Cancer Plan, aims to enhance cancer understanding, facilitate earlier detection, and optimize treatments. This initiative also focuses on improving the quality of life for cancer patients during and after their treatment. The four primary objectives of the Mission encompass:

- A deeper understanding of cancer.
- The prevention and early detection of the disease.
- Improved methods for diagnosis and treatment.
- Enhanced quality of life for patients and their families.

2.2. Cluster's objectives

The main objective of the cluster is to contribute to establish, scale-up and improve primary cancer prevention and early detection programmes, considering the specific needs of the target population, especially regarding economic, cultural and geographical conditions. Specific Objectives (SO) of the cluster are:

SO1. To implement and provide citizens with current evidence-based, tailored and affordable primary cancer prevention interventions at local, regional and national levels targeting known cancer risk factors and health determinants, chosen according to their sustainability, feasibility, cost-effectiveness, accessibility and affordability.

SO2. To identify and address the barriers avoiding the adoption and implementation of cancer prevention programmes in an accessible and affordable way.

SO3. To provide healthcare professionals and patient organisations with evidence-based information targeted at individuals and families on cancer prevention.

SO4. To collaborate with relevant stakeholders, including citizens, people at risk of cancer, patients, survivors, health professionals, payers and policymakers by involving them not only in the identification of barriers but also in the research and in the evaluation of its outcomes.

SO5. To develop policy recommendations aiming at informing policy and decision-makers.

SO6. To collaborate with responsible authorities at local, regional and national levels to facilitate evidence-based interventions to make them aligned with the corresponding commitments.

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3. Presentation of the projects participating to the cluster

The cluster includes the following six (6) projects, as given in the following Table 1.

Table 1 Prevention and Early Detection Cluster Projects

PROJECT ACRONYM	TITLE	GA No
CO-CAPTAIN	Cancer prevention among individuals with mental ill-health: co-adapting and implementing patient navigation for primary cancer prevention.	101104784
CPW	Cancer Prevention at Work: Occupational health surveillance in the implementation of prevention of infection-related cancer.	101104716
ONCODIR	Evidence-based Participatory Decision Making for Cancer Prevention through implementation research.	101104777
PIECES	Towards large-scale adaption and tailored implementation of evidence-based primary cancer prevention programmes in Europe and beyond.	101104390
4P-CAN	Personalized CANcer Primary Prevention research through Citizen Participation and digitally enabled social innovation.	101104432
PREVENT	Improving and upscaling primary prevention of cancer by addressing childhood obesity through implementation research-the PREVENT approach	101104618

3.1. Cancer prevention among individuals with mental ill-health: co-adapting and implementing patient navigation for primary cancer prevention (CO-CAPTAIN)

Cancer and mental health problems are major public health problems in Europe. More than 80 million people suffer from mental health problems, and around 4 million new cases of cancer are diagnosed each year. There is a link between mental health and cancer, with people with mental health problems having a higher incidence and mortality from cancer. In fact, cancer is one of the most common causes of death among this population, being the second cause of death after suicide. This is due to risk behaviours and difficulties in accessing fragmented health care systems. In this sense, evidence-based preventive strategies and improvements in health care could reduce cancer morbidity and improve the overall health of this disadvantaged population. There is a profound need to closely work with physical, mental, and care systems to collect further data and to apply and assess the effects of the implementation of primary cancer prevention interventions within this population.

In this framework, the CO-CAPTAIN project aims to provide an innovative solution based on the Patient Navigation Model to address health care inequalities for people with mental health problems in Europe. This model focuses on patient empowerment, removing systemic barriers, providing social support and ensuring access to primary prevention services. CO-CAPTAIN has the opportunity to co-adapt the Patient Navigation (PN) focusing on cancer prevention and test the resulting care model to navigate and support individuals with mental health problems through physical, mental, and care services to prevent cancer.

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For that, CO-CAPTAIN co-adapts the features of PN for primary cancer prevention tailored to the specific needs of individuals with mental ill-health and identifies implementation strategies for local communities in several pilot sites across Europe (Austria, Greece, Ireland, Poland and Spain). The pilot implementation is aimed at identifying and analysing potential facilitators and critical barriers for the PN for the primary cancer prevention implementation process, outcomes, and future dissemination and exploitation strategies. Special attention will be given to reducing the evidence-practice gap in health psychology and capturing the factors influencing behavioral change.

CO-CAPTAIN involves the collaboration of organisations with expertise in mental illness care in different regions of Europe, as well as academic institutions and local governments. The project uses scientific approaches and implementation frameworks and aims to reduce the burden of cancer and improve the overall health of people with mental illness, reducing costs in health and social care systems in Europe. In addition, it seeks to leverage integrated care pathways in cancer and provide policy recommendations for adopting the Patient Navigation Model across Europe. Thus, CO-CAPTAIN will provide the blueprint for transforming cancer prevention for all persons, integrating PN and delivering primary cancer prevention programs across health and care systems in the EU.

3.2. Cancer Prevention at Work: Occupational health surveillance in the implementation of prevention of infection-related cancer (CPW)

The overarching goal of CPW is to investigate the feasibility and performance of preventive interventions targeted toward major infection-related cancers within the framework of occupational health surveillance programs. Project seeks to furnish compelling evidence on the cost-effectiveness of innovative approaches for preventing infection-related cancers in the European population, as chronic infections represent a major cause of human cancer: on a global scale, they are responsible for an estimated 13% of human cancers. Helicobacter pylori (Hp), Hepatitis C virus (HCV), and Human Papilloma Virus (HPV) are responsible together for 75% of these cases, or 10% of total cancer burden [De Martel et al., 2020].

Occupation health surveillance is mandatory in all European countries: although the mechanisms of its implementation vary between the countries, these programs are, in general, aimed at diagnosing and preventing work-related diseases. Therefore, occupational cancer prevention has been a component of occupational health surveillance. In recent years, however, there has been a movement towards including in occupational health surveillance aspects of health promotion, which are not occupational in a strict sense. This approach stems from several considerations: i) the contact between the worker and the health professional in charge of the surveillance can be seen as a privileged opportunity for health promotion in general; ii) through the worker, the health promotion initiative may reach other groups of the population; iii) because of the periodic nature of the visits entailed by the occupational health surveillance, it is possible to efficiently implement follow-up mechanisms.

The conceptual framework of CPW Project is based on the incorporation into on-going occupational surveillance schemes of primary prevention programs against infection with Hp, HCV and HPV. Pilot studies will be conducted in four European countries: Italy, Slovakia, Spain and Romania. The CPW Project aims to cover the following objectives: conduct pilot projects to evaluate the effectiveness, including cost-effectiveness, of integrating primary prevention interventions for Hp, HCV, and HPV into existing occupational surveillance systems among high-risk populations; assess the broader impact of these interventions beyond the workers directly involved; and identify barriers and challenges hindering the implementation of these interventions.

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3.3. Evidence-based Participatory Decision Making for Cancer Prevention through implementation research (ONCODIR)

Colorectal cancer (CRC) ranks among the most prevalent cancers, with its rising incidence often linked to negative health habits, particularly in populations with lower socioeconomic status. ONCODIR tackles CRC by employing a variety of research methodologies, encompassing health policy analytics, social and behavioral sciences, AI-enhanced, retrospective data analysis, and decision support systems. These methods aim to develop both evidence-based cancer prevention programs and cutting-edge, personalized AI-driven prevention strategies. ONCODIR is also focused on assessing the cost-effectiveness, affordability, and overall financial benefits of its prevention programs. This involves exploring financial models that balance costs and stimulate demand, thereby improving CRC prevention efforts.

ONCODIR provides a seamless technological ecosystem, grounded in solid AI reliability and privacy safeguards, to implement recommendation services. These services will be refined through input from citizens, health policy professionals, and Social Sciences and Humanities (SSH) experts during three design thinking workshops. SSH research will study and consider factors like individual life circumstances, dietary and social patterns, as well as considerations of economics, sociology, local/regional cultural identities, and ethics.

The project's outcomes will undergo testing in three Laboratory Integration Tests (LITs) and three Large-scale Intervention Pilots (LIPs) across five EU member states, with direct participation from medical scientists, healthcare providers, foundations, and consortium experts. The ONCODIR consortium, known for its high-quality research capabilities, brings together partners from various disciplines, including research, technology, and SSH. The comprehensive work plan of ONCODIR is designed to achieve its objectives and produce viable, policy-supportive results with considerable potential for practical application.

3.4. Towards large-scale adaptation and tailored implementation evidence-based primary cancer prevention programmes in Europe and beyond (PIECES)

There are various Primary Cancer Prevention (PCP) programmes and varying theories of change available with proven effectiveness available. Decision-makers and implementers face the challenge of 1) selecting the most appropriate and suitable programs among a pool of experiences in different areas and settings that yielded heterogeneous results, 2) tailoring them to the local context and stakeholders involved, and 3) developing an action plan for effectively implementing the selected and adapted PCP program. The lack of guidance and support for this complex and time-consuming process lead to two undesired outcomes: 1) the selection of ineffective or poorly adapted PCP programmes and, 2) applying ineffective implementation strategies not targeting local and context-dependent barriers to the implementation. Either of the two scenarios is likely to hamper the effectiveness of these PCP programs in real-world settings, thus generating inefficiencies due to assay-error approaches and failing preventing the onset of new cancer cases.

PIECES will overcome the current scenario by 1) developing a specific framework for adapting and implementing evidence-based PCP programs and, 2) providing implementers with a toolkit for selecting the right components and assembling all the pieces for a successful implementation of the PCP programs. The implementation toolkit (i.e., Primary Cancer Prevention – Implementation Toolkit; PCP-IT) will be theory-based and includes a generic work process, evidence-informed materials, and methods necessary for tailoring implementation strategies to the local context. Various comprehensive repositories will be integrated in PCP-IT: 1) detailed information about currently available PCP programmes including their evidence-base, 2) a comprehensive list of barriers associated with implementing PCP programmes, and 3) evidence-informed implementation strategies to target barriers.

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As such, the main purpose of the PIECES project is to select, adapt, and implement existing evidence-based programmes to improve implementation out outcomes and by that, improve reach and effectiveness of primary cancer prevention programmes in real-world settings. The consortium addresses a wide range of risk factors and focus on the specific behaviour change mechanisms that promote healthy behaviours associated with a reduction of cancer incidence among the European Union (EU) population and beyond. The main modifiable risk factors that we are aiming to tackle in the project include: 1) tobacco smoking and exposure to second-hand smoke, 2) Alcohol consumption, 3) poor physical activity, 4) HPV infection, 5) sun exposure, and 6) diet.

PIECES brings together a multidisciplinary team of primary cancer prevention researchers and clinicians, implementation scientists and practitioners, behavioural change experts, stakeholder representatives, and a diverse set of implementation sites in Albania, Australia, Germany, Netherlands, Italy, Spain, United Kingdom, and Ukraine. The implementation sites have a prominent regional or national leading role in developing and implementing evidence-based PCP programmes. The geographical diversity and multiplicity of socio-cultural realities of the implementation sites and the heterogeneity of the PCP programmes provides the perfect environment to gain in-depth understanding about successful implementation of PCP programs.

A multi-site case comparison study design with pre/post-test of implementation outcomes will be applied to generate in-depth knowledge about the performance of PCP-IT. A time horizon of two years will be taken to be able to assess change over time. Similarities, differences, and patterns across the cases will be investigated using a Realist Evaluation approach with various sociological and implementation theory derived hypotheses about the mechanisms of action (of PCP-IT).

3.5. Personalized CANcer Primary Prevention research through Citizen Participation and digitally enabled social innovation (4P-CAN)

Primary cancer prevention is widely recognised as a shared responsibility involving citizens, healthcare professionals, and decision makers. The EU-funded 4P-CAN project seeks to gain a comprehensive understanding of the complex factors influencing cancer risk at the national, community, and individual levels. Drawing from a multidisciplinary approach, including insights from the European Code Against Cancer, implementation research, social sciences and humanities (SSH), behavioural sciences, and innovative technology, the project aims to develop personalised tools for primary cancer prevention in Central and Eastern European countries through Living Labs. It also aims to implement tailored communication campaigns on cancer prevention. Integral to the broader EU Cancer Mission, the project ultimately aims to reduce cancer risk factors, improve prevention, and address inequalities.

With a strong belief that primary prevention of cancer represents a collective responsibility (citizens, professionals, decision-makers), during a 4-year period, 4P-CAN builds on an innovative vision to understand the complex system that surrounds the citizen, the person, and how it increases the risk for cancer on three major levels - macro (at the national level), meso/mezzo (at the community level) and micro (at the individual level). Following the European Code Against Cancer recommendations as a narrative reference and combining implementation research (including economic sciences), social sciences and humanities (SSH), together with behavioral sciences, and innovative technological approaches, 4P-CAN ultimately delivers new personalized tools for primary prevention of cancer in Central and Eastern European countries from the consortium. The co-created knowledge is then used to personalize the primary prevention interventions through Living-labs and implement personalized communication campaigns on cancer prevention.

The project will focus on some of the main modifiable risk factors for cancer occurrence: smoking, alcohol consumption, physical inactivity, excess body weight (overweight and obesity), HPV and HBV infections preventable through vaccination, as well as environmental pollution (including radon), and the understanding of the barriers in front of the policy implementation and individual adherence to healthy behaviors in countries

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from Eastern Europe (Romania, Bulgaria, Republic of Moldova, North Macedonia, Montenegro, Ukraine), to improve as a consequence the primary prevention activities and reduce the inequalities.

Altogether, 17 organizations from 11 different countries are getting together to achieve these goals, i.e. Balkan countries (EU Member States and non-EU Member States), part of CEE: Romania, Bulgaria, North Macedonia, Montenegro; Republic of Moldova and Ukraine; and Western EU countries (Portugal, Italy, France, Ireland, Belgium).

3.6. Improving and upscaling primary prevention of cancer by addressing childhood obesity through implementation research – the PREVENT approach (PREVENT)

Obesity is considered as a global epidemic affecting almost all countries, with trends showing that further increase of the worldwide prevalence is expected in the future. One in three children of ages from 6 to 9 in Europe is overweight or obese. Childhood obesity is highly related with a range of serious consequences for the health life in childhood and a higher risk of premature death and carcinogenesis in adulthood. According to the US Centers of Disease Control and Prevention (CDC), being overweight or having obesity increases the respective risk of getting more than thirteen types of cancer.

Several clinical trials and studies indicate that early weight control management, especially during childhood and adolescence, have a negative association with an increased cancer risk in adulthood. Epidemiological studies indicate that excess body weight is associated with different types of cancer due to the metabolic syndrome. PREVENT proposes multi-actor and context aware primary intervention mechanisms for weight control management in childhood/adolescence to avoid cancer development in the future. The delivered new policies are highly personalized and thus tailored to specific user needs, the cultural environment and the social context since new implementation research actions, such as co-creation, active behavioural change or self-evaluation are foreseen during the Project.

Overall, PREVENT is expected to reduce weight excess by more than 20%, and therefore to play a significant role towards the battle of cancer within Europe. This will be achieved by establishing three different implementation ecosystems across Europe (Greece, Sweden and Catalonia) that they include: i) school communities; ii) healthcare professionals; iii) regional/national policy makers in both healthcare and education; and iv) civil associations with respect to obesity and cancer. The pilot ecosystems increase effectiveness in counselling, provide targeting guidelines and improve upscaling.

PREVENT promotes outreached upscaling activities targeting more than 10.000 schools and more than 3,3 Million of students of age nine to six. The project aims to establish a framework of continuous assessment and validation of the new policies towards the development of evidence-based optimised strategies for upscaling and large adoption of the project's interventions and outcomes.

4. Research & Innovation Thematic Areas per project

4.1. CO-CAPTAIN

Based on implementation science know-how and using the Consolidated Framework for Implementation as well as the Research and the Reach, Effectiveness, Adoption, Implementation and Maintenance frameworks, the Co-CAPTAIN project aims to reduce the gap in health inequalities for people with mental ill-health by reducing cancer burden and improving overall health, which will, in turn, reduce associated costs across health and social care systems in Europe. Moreover, the Co-CAPTAIN project aims to harness the transformative potential of the integrated care pathways in cancer as well as provide health and social care policy recommendations for the adoption and implementation of the Patient Navigation Model across Europe.

4.1.1 Scaling the Patient Navigation Model

The Patient Navigation model had demonstrated a huge transferability potential at the healthcare system level (national scale). Its adaptation to primary prevention of cancer for populations affected by mental disorders will overcome barriers to timely treatments, increasing prevention resources and health promotion devoted to a highly needed group.

CO-CAPTAIN focuses on delivering a cost-effective and affordable co-designed patient navigation model for people with mental illness focusing on individual and organisational risk factors closing the gap in the implementation of PN, co-designing and implementing patient navigation and enhancing Health and Care Systems' capacity at European and country level to design, implement and supervise cost-effective and affordable cancer prevention strategies.

4.1.2 Health inequalities

CO-CAPTAIN objectives relay on the mission statement of the European Guide on Quality Improvement in Comprehensive Cancer Control by the EU Cancer Control Joint Action for cancer burden reduction but also reduce cancer care inequalities. CO-CAPTAIN shares the same principles as the European plan to fight cancer, aiming at reducing cancer care inequalities between and within the Member States. As stated in the "Europe's Beating Cancer Plan, Let's strive for more", CO-CAPTAIN meets the need for person-centred models of care prevention delivery and reduction of cancer inequalities.

By focusing on equal access for all, CO-CAPTAIN delivers proven effective person-centred Patient Navigation to overcome cancer care inequalities and facilitate cost-effective primary cancer prevention for individuals with mental ill-health. CO-CAPTAIN has the unique opportunity to capitalize multiple voices in each pilot site to explore the CO-CAPTAIN model and to work within organisations and services for the identification of early implementation barriers/facilitators. Careful consideration is given to ensure equal representation and diversity among research participants as described later. The Consolidated Framework for Implementation Research (CFIR) and The Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) frameworks used within the implementation science will be used to close this gap as a way of reducing cancer burden while optimizing resource utilization across healthcare systems in EU.

4.1.3 Co-creation

CO-CAPTAIN consortium adopts the following definition of co-creation provided by MHE: "*A collaborative approach involving all actors in mental health working together on an equal basis to develop and implement*

policies, services and communication that foster positive mental health according to the psychosocial model and human rights-based approach". In this framework, CO-CAPTAIN stakeholders including 25 individuals with mental ill-health, 10 caregivers, 10 care team members, 5 representatives of mental health organisations and 5 service managers will participate in co-design sessions within each pilot.

The Evidence Based Quality Improvement (EBQI)[54] model guides the strategy development process to identify and analyse the potential facilitators and critical barriers for the Patient Navigation for primary cancer prevention implementation process. EBQI is rooted in the principles of participatory research by bringing together key stakeholders to adapt evidence-based practices for local contexts and identify implementation strategies. Moreover, the CO-CAPTAIN consortium, in a co-creation approach involving all key stakeholders, will define the standards on PN in the cancer care continuum for individuals with mental ill-health by using Delphi techniques to build international consensus among different key informants (such as existent navigators, public health experts, nurses, social workers & psychologists).

Thus, COCAPTAIN will foster evidence on the implementation of co-creation in the implementation research within EU-large interventions.

4.1.4 Social impact

Health, both physical and mental, is co-determined by social, cultural, environmental, administrative/political, behavioural, and biological factors; all these interact in a complex causal network. The complexity of the relations between all these co-determinants requires addressing them from an epidemiological and sociological perspective.

CO-CAPTAIN will contribute to society by promoting a cost-effective intervention within a socio-ecological and multi-sectoral approach, thus:

- Fostered self-efficacy and self-care and raised capacities and skills for developing healthy coping mechanisms, and beneficiaries' self-management of concomitant NCDs, if any. Also, reduced severe acute crisis due to suicidality, self-harm and intoxication.

- Thus, leading to an enhanced and cost-effective self-management of health evaluated through the HER (health records) and, specifically, the number of diagnosed exacerbations, all health settings (Emergencies, acute units, hospitalisation, primary care). Quality of life will be also considered:

- Improved QoL, thus, increased QALY. According to the literature, other potentially related impacts of QoL are the reduced absenteeism and increased social, labour, and public life participation.

- Improved policies and decision-making processes enlightened by further knowledge and evidence about social determinants of health, impacting and increasing communities' resilience.

- Better-informed social and healthcare providers about commonly reported issues with patients with mental suffering dismissing the barriers experienced by those to access appropriate care on time.

4.1.5 Health policies

CO-CAPTAIN will provide proven and evidence-based guidelines and policy recommendations for addressing the health and social inclusion, as a whole, specifically tackling life-style factors, mainly diet and nutrition, alcohol and tobacco use and embodied coping mechanisms. In fact, one of the general aims of the project is to implement a large-scale pilot of primary cancer prevention in 5 different health and care systems in Europe in order to inform the blueprint for the transformation of policies. In this context, the project strongly encourages the integration of the end-users' voices and opinions in the management and decision-making process by means of participatory strategies that will be used to ensure the real meeting of their real needs and concerns since the project starting.

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4.1.6 Integrated approach

The conclusions of the project could hence be a first step towards a "whole person" approach across EU health and care systems adopting integrated care principles understanding the needs of individuals with mental ill-health, playing an important role in reducing the burden of non-communicable conditions such as cancer. In this regard, the results of CO-CAPTAIN development could contribute to the adoption of PN for the whole cancer continuum for individuals with mental ill-health.

4.1.7 Behavioural change

It is necessary to interweave the evidence-practice gap with the implementation science for fitting well into the organisational structures. CO-CAPTAIN will not just focus on capitalising on the potential of the evidence generated by the intervention but will use CFIR and RE-AIM frameworks to capture the factors influencing behavioural change alongside the innovation proposed by CO-CAPTAIN. CO-CAPTAIN will also evaluate the user-centeredness and efficiency from the point of view of the implementation of the interventions promoting evidence of the uptake of healthier behaviours and healthier coping mechanisms, reducing harmful and hazardous habits, and tackling jointly physical and mental health to promote the accessibility to high-quality care. The results of the CO-CAPTAIN project will provide rich evidence (evaluation deliverable) and recommendations on the adoption and upscaling of the Patient Navigation (PN) addressing lifestyle factors.

4.2. CPW

The CPW main innovative aspect lies in evaluating the feasibility and efficacy of preventive interventions targeting infection-related cancers within the framework of occupational health surveillance programs at a large scale. Through comprehensive pilot studies, CPW aims to assess the integration of primary prevention interventions for Hp, HCV screening, and HPV vaccination into existing occupational surveillance systems among high-risk populations, including healthcare workers, but also metal, retail, manufacturing, and financial sector workers. This approach leverages established physician-patient relationships and existing health infrastructure, potentially offering a highly cost-effective solution. Drawing insights from the pilot projects' outcomes, these plans will be tailored for implementation in participating centers and extended to other EU countries, aligning with established frameworks for implementation science. Additionally, exploratory interviews with occupational physicians and managers will delve into key aspects to inform the implementation strategy effectively.

4.2.1. Gastric Cancer Prevention through Helicobacter Pylori Screening and Treatment

The CPW project introduces an innovative approach to Hp screening, integrating it into routine occupational health surveillance with rigorous occupational physician training ensuring effective Hp screening implementation. The CPW approach includes screening for HP infection, counseling on eradication, and facilitating access to specific medical care for Hp-positive individuals and their household members. Moreover, the CPW Project recognizes the importance of gathering detailed data on Hp infection prevalence across different occupational groups and exploring potential interactions between occupational risk factors and HP infection. Collaborating with national cancer mission hubs and stakeholders, it seeks to disseminate findings, foster policy dialogue, and drive further research actions related to Hp prevention, ultimately aiming to reduce the Hp-related gastric cancer burden and enhance public health outcomes.

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4.2.2. Preventing Liver Cancer through HCV Screening and Treatment

The CPW project's innovative plan for HCV screening builds upon the proven success of micro-elimination approaches in high-risk populations. CPW's approach will focus on preventing Hepatitis C infection-related cancers by implementing WHO guidelines for testing, confirmation, and treatment by extending this concept to occupational settings. CPW aims to reduce HCV underdiagnosis and ensure timely treatment of existing infections, which is essential for the primary prevention of hepatocellular carcinoma. CPW model emphasizes expanding screening beyond high-risk workers, with occupational physicians playing a pivotal role in increasing acceptability, raising awareness of HCV-related liver cancer, and highlighting the safety and efficacy of existing treatments. Through patient linkage to care and follow-up, we seek to catalyze progress against HCV and its related cancers within these settings, ultimately aiming for their elimination.

4.2.3. Prevention of Cancers Associated with HPV Infection

Introducing occupational interventions for HPV-related cancer prevention, particularly in countries where such interventions are lacking, presents an innovative approach. This includes theory-based interventions to enhance communication about HPV prevention and vaccination among occupational healthcare providers. The project aims to reduce the incidence of HPV-related cancers by raising awareness and promoting participation in preventive activities, including HPV vaccination, particularly in middle-income countries in Europe. By providing insights into designing and implementing strategies to support and empower occupational health surveillance programs, including HPV vaccination, this study seeks to enhance HPV control. Strengthening communication among healthcare providers and workers regarding HPV prevention and vaccination will be prioritized, potentially addressing vaccine hesitancy.

4.2.4. Cost-Effectiveness and Replicability of Interventions

The CPW seeks to identify the cost-effectiveness advantages of using occupational health surveillance for implementing broader interventions. It aims to provide robust evidence for decision-makers, potentially influencing future research and practical initiatives in occupational health surveillance and cancer prevention. Cost-effectiveness analysis (CEA) is a crucial tool in evaluating the economic viability of health interventions, comparing the costs incurred against the benefits gained in terms of improved health outcomes. This analysis plays a pivotal role in determining the success of health interventions and will be integral to assessing the piloted interventions within the CPW Project. The overarching objectives of the CEA in this Project include:

- Evaluating the cost-effectiveness of the interventions in comparison to scenarios with no intervention and interventions targeted at the general public.
- Identifying and assessing the key factors that influence the cost-effectiveness of the interventions, considering both the intervention's design and structural conditions.
- Assessing the potential for scaling up the interventions, including their applicability across different industry sectors and Member States.

4.2.5. Health Capital and Behavioral/Sociocultural Barriers

The CPW aims to comprehend how individual resources, influenced by emerging perspectives of health capital, impact engagement in occupation-based interventions. Utilizing health capital theory, it explores economic, social, cultural, and symbolic resources shaping individuals' roles in the health domain. In the context of occupational-based interventions, the Project delves into the complexities of individual resources influenced by

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emerging perspectives of health as personalized and privatized capital. This approach holds promise in navigating the increasing personalization of healthcare and rising health inequalities, particularly in addressing the diverse needs of workers. Health capital serves as a lens through which to examine how these resources shape interactions with occupational-based cancer prevention interventions, healthcare professionals, and peers. To effectively utilize health capital in cancer prevention, the CPW Project emphasizes the need for a nuanced understanding of the mechanisms underlying behavioral and sociocultural barriers and facilitators. This necessitates operationalizing health capital into an assessment tool, acknowledging that disparities in resource distribution significantly influence the dynamics of cancer prevention programs. By unraveling these complexities, the Project aims to enhance understanding of how individual resources intersect shape cancer prevention practices, thereby informing more effective cancer prevention strategies.

4.2.6. Collaboration with National Cancer Mission Hubs

Engaging with national cancer mission hubs established through EU-funded initiatives facilitates policy dialogue and research actions related to cancer prevention.

4.3. ONCODIR

ONCODIR highlights the significant commitment of policymakers to unite European countries in their efforts to substantially reduce the enormous cancer burden. It aims to integrate various partners from different fields to provide a holistic overview in terms of budget and gender inequities, openness, and compliance with citizens' rights, as well as their impact, based on a carefully selected set of criteria and indicators. In this direction, ONCODIR aims to address these challenges through multifaceted, interdisciplinary co-creation activities by implementing tools and methodologies for a) risk-based stratification for citizens, b) integrated decision support tools for clinicians, and c) intelligent monitoring tools for policymakers. All the above will also contribute to personalized prevention, successful interventions, actions, and implementation plans by incorporating the views and perspectives of citizens/patients, medical experts, and policymakers through a participatory co-design approach, reinforced by open innovation and FAIR data that focuses on measuring the interventions' impact and deriving important insights.

4.3.1. Implementation Research

The ONCODIR approach will build upon the trust and complementary capacities of partners from various disciplines and sectors to design suitable evidence-based prevention programs. Thus, they will be able to strategically overview information regarding the number of CRC cases, mortality rates from a macro (national) to micro (regional/local) level, etc. The aim is to implement a systematic framework based on structural and behavioral interventions, which will be monitored by policymakers to measure their effectiveness and impact across the studied EU countries. Behavioral interventions aim to improve citizens' health through educational activities that equip them with the necessary information to make health-beneficial decisions, requiring limited political involvement and commitment. Structural strategies promote healthy options through changes in the context of their occurrence, irrespective of the individual's education and socioeconomic level, focusing on environmental factors influencing risk behavior. The most promising ideas will be discussed with and evaluated by regional authorities and policymakers to ensure the interventions are directed appropriately.

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4.3.2. Co-design/creation

In ONCODIR, to enhance the participatory process, a user-friendly, design thinking-inspired communication platform will be implemented. This platform will promote collaboration, allowing researchers, stakeholders, and end-users to co-design the implementation of prevention interventions. Through this co-design approach, potential gender or ethical limitations will be addressed early on, facilitating increased acceptance rates for interventions. ONCODIR will encourage active participation and co-design via a Living Lab process, fostering a creative and participatory policy-centric dialogue for evidence-based policymaking. Dedicated workshops, ensuring equal participation across genders, will gather requirements and identify potential challenges for open innovators, who will then seek solutions leveraging open data. A stakeholder participatory, iterative approach will co-determine the system architecture, thus ensuring user acceptance of the platform while considering ethical, gender, and legal aspects.

4.3.3. Active Behavioural Change

Even though there is significant potential in mobile apps to improve citizens' and patients' quality of life (QoL) by providing recommendations with the ultimate goal of reducing colorectal cancer (CRC) morbidity and mortality, the quality and content of these apps remain uncertain. Thus, more effective strategies for preventative measures based on geographical and socioeconomic inequities are required. The ONCODIR Mobile App will obtain a comprehensive understanding of the holistic needs of all subgroups, including survivors, exposed to cancer, while providing more targeted awareness campaigns (beyond the project). citizens can provide feedback on specific policy measures through a bidirectional interaction, facilitating participatory decision-making. Through the mobile app identifying high-risk groups or groups with geographical and socioeconomic inequities will allow for more effective preventative measures.

4.3.4. Social Impact

Through Mapping of Best Practices and Policies in Cancer Prevention Implementation Research, focusing on evidence-based policies the ONCODIR Implementation Research Framework will promote community-based, context-sensitive research and scale-up implementation from a bottom-up perspective. This framework aims to develop a methodology that encourages citizen participation in the ideation of new policies, supporting participatory policymaking from another angle. The synergy of both bottom-up and top-down implementation research frameworks for CRC prevention will culminate Replicable Primary Prevention CRC Programmes for Regional & National Authorities for the Adoption of the ONCODIR CRC Prevention Methodology by EU countries. Furthermore, the participation of external stakeholders alongside consortium partners in the during the Co-design Workshops will create opportunities to upscale prevention ideas through social, open, and gender-based innovation in an ethical manner.

4.3.5. Health economics

An analysis of health economics will be conducted, along with Health Technology Assessment (HTA), to evaluate and test the financial viability of the proposed novel CRC methods for various European national healthcare systems. Additionally, innovative financial schemes will be investigated to enhance our method and achieve streamlined cost-effectiveness. By analyzing public-private partnerships (PPPs), further cost reductions can be achieved on a large scale. The role of insurance companies in incentivizing mechanisms (e.g., reduced insurance fees for those who get screened) and innovative financial schemes will be explored from the consistent

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adoption of affordable interventional measures and adherence to CRC prevention programs. ONCODIR will evaluate life expectancy using QALYs/DALYs as metrics for calculating healthcare costs and measuring the impact of clinical interventions with precision through the Financial & Life Expectancy Evaluation of the ONCODIR Solution as a whole.

4.3.6. Policy analytics

ONCODIR will initially incorporate aggregated retrospective results from various data sources, which will be analyzed to identify significant variables from diverse origins (clinical, socioeconomic, lifestyle). This analysis aims to enhance our understanding of how various factors and conditions differentially affect the CRC risk level and its prevention across EU countries. Throughout the project, we will focus on socioeconomic data to expand the European Cancer Inequalities Registry from national (macro-level) to regional (micro-level) information, comparing urban vs. rural, educated vs. non-educated, minorities & vulnerable groups, rich vs. poor, gender, etc Subsequently, ONCODIR will define a set of PROMs/PREMs to evaluate and provide feedback on different policy measures and treatment plans, through a mobile app, reinforcing bidirectional interaction between policymakers and patients/citizens. The outcomes will be displayed through rich visualization within the Evidence-based Policy Analytics Dashboard. Policymakers will be able to analyze anonymized information from provided questionnaires, considering a series of other important factors such as socioeconomic status. Thus, the methodology will create a direct link, generating evidence data for evaluating the performance of existing and forthcoming policies.

4.3.7. Living Labs

ONCODIR-related Living Labs will be established to ensure the project's widespread visibility and maximize its impact on European societies, the research community, healthcare professionals, citizens, and patients. All necessary materials will be developed to create an effective "communication kit" available to all partners. This kit will be used to raise awareness of the project and assist in the necessary actions. The outcomes will focus on policymaking and suggestions by the ONCODIR tools towards National/Regional cancer strategies and the corresponding incentivizing mechanisms, based on clearly stated evidence for open and gender-based innovations for CRC prevention.

4.3.8. Trustworthiness

ONCODIR will cater to ongoing user stratification through an iterative recommendation process that exploits AI-based early predictive-warning digital tools and multimodal analytics. This process will support evidence-based clinical decisions for clinicians and policymakers. By employing a data-driven approach that utilizes analytic Machine Learning (ML)-based AI tools, fuse Big Data from heterogeneous sources and disease stages to enhance predictions of future disease states of patients based on their current clinical state and available history. The AI tools developed for ONCODIR will be suited for the analysis of multidimensional data, including diverse data types such as cancer risk factors, cancer prevalence in the EU countries, socio-economic information, behavioral data, and environmental stressors in specific regions. Clinical experts will contribute a set of semi-empirical rules based on evidence to feed the AI tools and ONCODIR recommendation engines in a trustworthy manner. The results extracted from the intelligent analytics will be shared with policymakers and healthcare professionals to unveil health determinants and factors associated with socio-economic inequalities, potentially correlating with environmental and other stressors. This effort will emphasize social values and the efficient and cost-effective use of resources for preventative measures. ONCODIR will be offering trustworthy clinical recommendations while

minimizing costs. Policymakers will receive information about best practices and suggestions for updating National Cancer Plans with specific evidence-based measures. They will also have access to rich visual insights from intelligent analytics, which fuse information from heterogeneous sources, enabling them to suggest more targeted and accurate.

4.4. PIECES

PIECES' approach is based on the premise that contextual factors can make or break an implementation. Implementation science has developed various frameworks regarding implementation outcomes and process models, which consists of describing and/or guiding the process of translating research findings into practice to increase chances of success. The use of those frameworks and theories is a rational approach to reduce cancer prevention inequalities and reduce the burden of cancer in Europe among all groups, and especially amongst the most vulnerable. Findings and approaches from implementation science can be useful to overcome general barriers; tailored implementation may add value considering that the implementation of evidence-based PCP programmes in dynamic and heterogeneous contexts raises barriers that differ from setting to setting and time to time. One-size-fits-all implementation strategies likely do not exist, and strategies require tailoring to the dynamics and requirements of the local context.

4.4.1. Implementation science: tailored implementation

Tailored implementation consists of getting relevant stakeholders together to identify barriers in local context, match those to evidence-informed strategies, adapt interventions into workable action plans, apply plans and evaluate outcomes. The tailoring process can be generic and applied in different settings but should lead to strategies that are workable and make sense in the local and cultural environment at a given moment in time. The concept of tailored implementation is a relatively new and recent advance in implementation science, and data collected to date indicate a significant but modest effectiveness in improving implementation outcomes.

An example of how to translate research into practice by tailoring implementation strategies feasibility considering the cultural and social environment has been recently proven with the ItFits-toolkit. Funded by Horizon 2020, this toolkit was developed and tested for effectiveness for the implementation of evidence-based eMental health interventions in 12 mental health organizations across Europe and in Australia. The ItFits-toolkit provides an online stepped approach that is infused with scientific evidence about barriers and strategies. The ItFits-toolkit was found to be effective and usable.

What is lacking in this approach and prior to developing tailored implementation strategies, is a proven generic process for adapting PCP programmes to achieve an optimal fit with the context and setting it is to be implemented in, without diminishing their effectiveness. This is a common and long-standing issue in translating and implementing medical and public health interventions to practice. Once the effectiveness is established and the EBP's are finding their way to practice, they get adapted, either intentionally or unintentionally, to fit within the setting it is implemented. However, it is often unknown and unclear what the specific working mechanisms of a programme are and thus there is little guidance in what can be changed and what should not to maintain effectiveness or without the need to prove its effectiveness in a specific setting and target population.

Building on the existing toolkit for tailoring implementation strategies, PIECES will deliver a comprehensive, generic, yet flexible online toolkit that includes guidance for both tailoring of PCP programs to improve its local fit and developing specific tailored implementation strategies for implementing the adapted PCP programs.

4.4.2. Methodology: Realist Evaluation

While we know that tailored implementation is effective, be it moderate, we do not know the specific mechanisms by which it is effective and in which context it can or cannot be used. For that reason, we will apply a multi-case comparison study using a Realist Evaluation approach. This methodology is specifically focused on studying what works for whom in what circumstances. The focus of the study lies on implementers using the PCP-IT. Starting from the logic model behind the toolkit (i.e. the theory of change, or core functions by which the toolkit achieves its effects), we will develop statements that hypotheses relationships between characteristics of the context in which the toolkit, the mechanisms by which the toolkit operates, and outcomes we can observe. These CMO configurations will be validated using a mixed-methods approach using both quantitative data on implementation outcomes as well as in-depth process evaluation data. This will allow us to confirm, refute, or refine the hypothesized relationships between unique characteristics of the context, the mechanisms, and expected outcomes the toolkit contributes to in selecting, adapting, and implementing PCP programs for various risk factors in practice.

4.4.3. Communities of Practice

As part of the toolkit, a community of implementation practitioners will be established. Note that this community is focused on implementers; staff responsible and engaged in implementing interventions, programs, and innovations into routine practice. The purpose of the community of implementation practitioners is to enable mutual learning through exchange of ideas, experiences, and knowledge of implementation projects. It is an international community which will engage online through a forum to raising ad-hoc questions and answers from the community as well as thematic topics such as identifying barriers, methods for involving stakeholders, or selecting implementation strategies. Moreover, the forum will be an integral part of the PCP-IT toolkit which will also allow showcasing and browsing existing implementation projects in the toolkit.

4.4.4. Active Behavioural Change Model

Although not specifically the Active Behavioral Change Model, in PIECES, behavioral change is central. The PCP-IT aims to support behavioral change in three ways. First, through supporting the implementation of PCP programs which mostly include behavioral change techniques. Secondly, the strategies that can be applied to implement the PCP programs, often include behavioral change methods, such as audit and feedback, incentives, and rewards, etc., which are based on specific behavioral change techniques and theories. Third, the toolkit facilitates change in behavior of implementers, the toolkit users themselves in terms of motivation and self-efficacy. This is mostly achieved by providing a stepped work process while balancing flexibility and structure and increasing implementation skills and knowledge through learning.

4.4.5. Social Impact

PIECES offers an evidence-based solution aimed to improve the implementation processes and outcomes related to implementation of PCP programmes. With this tool and through successful implementation of PCP programs in various regions in Europe, the project contributes to decreasing the incidence and prevalence of cancer in Europe. Briefly, the project is expected to overcome current trends of poorly implemented EBPs for primary prevention of cancer in the following ways:
- Building on existing databases, creating a comprehensive repository of PCP programmes and effective implementation practices with theories of change and appraisal of evidence.

- Providing a cancer-specific theory-based framework for upscaling and tailoring PCP programs taking into account the local context and stakeholders involved.
- Focusing on the most prevalent and impactful modifiable risk factors, including tobacco, exposure to second-hand smoke, alcohol, physical activity, and sun exposure.
- Tailoring local contexts: PIECES will ensure that the interventions selected are culturally sensitive and more likely to be effective and accepted in the target populations.
- Promoting advanced systemic change at the policy, administration and clinical level that will veil for the adoption, correct implementation, evaluation, and sustainability of cancer prevention interventions. Notably through the involvement of policy and advocacy partners in the consortium as well as through the implementation sites' networks of stakeholders in national and regional settings, the policy and decision-making processes at micro, mesa- and macro levels are targeted.
- Advancing implementation research at the European level: PIECES will enhance the understanding and implementation of evidence-based interventions.

Long-Health Outcomes: PIECES, like the rest of the Cluster projects, is ultimately concerned with improving long-term outcomes to reduce the burden of cancer in the EU. PIECES deliverables are expected to accelerate cancer prevention programmes, break current bottlenecks and barriers in their implementation and reduce inequalities in access to evidence-based tobacco, alcohol, poor physical health, exposure to UV, and diet prevention programmes.

Thus, PIECES will contribute to the EU Cancer Mission Plan to reduce the burden of cancer achieving the EU overall goal of 3 million people living longer and better by 2030. Moreover, PIECES is aligned with Sustainable Development Goals, in particular with goals 3.4 and 5 "Ensure healthy lives and promote well-being for all ages" intended to reduce the burden of non-communicable diseases through prevention of promotion of well-being and through promoting gender equality and empowerment of all women. In Europe, 80% of the burden of disease is caused by non-communicable diseases and cancer is responsible for 1.3 million deaths annually (26% of total mortality) although incidence and mortality rates are uneven among population groups with low socioeconomic groups and female as a specific vulnerable target groups.

4.4.6. Open science practices

The approach of PIECES towards open science practices is fully aligned with the Horizon Europe guidelines and goes beyond mandatory practice by deploying a strategy that seeks knowledge-sharing and cooperative work. This strategic approach will be defined in the first deliverable of the project D7.1 Management handbook on M4. Data received from this project will be stored according to the FAIR principles in order to be Findable, Accessible, Interoperable and Reusable. In order to make our data findable, the final datasets will be assigned a globally unique persistent identifier (e.g., DOI) described with rich metadata (including the identifier). The metadata of the project and information on where to find the original data will be found in a data repository (such as DataverseNL). The study part of the project will be registered on clinicaltrialsregister.eu and PROSPERO (for systematic reviews). Accessibility will be ensured by the fact that processed data, without identifiable information, will be available on request from the researchers. Due to privacy, sensitive data will receive a unique code (serving as a proxy for an identifier) and be stored an offline archive for storage of sensitive information. This type of information will only be available for authorized individuals. The interoperability requirement will be achieved by following the SPIRIT guidelines, which will guide the creation of the metadata scheme providing information about the research data. The metadata will use a formal, accessible, shared, and broadly applicable language for knowledge representation and vocabulary, and include references to all relevant (meta)data. Finally, to reach reusability, the project will use a purpose-built software tool (central database system) allowing also for following an audit trail, will be used for creating and coding reusable data. The research process will be well-documented and quality assurance measures

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will be in place. A replication package will be provided according for archiving data for replication and in accordance with requirements for medical research.

The Scientific Coordinator and the Scientific Committee will oversee the process covering the following areas: 1) Early and open sharing of research: all publications (including study protocol and research outcomes) will be submitted to open access repositories. The selection of scientific journals will include those that accept preprints or early publications in repositories; b) Research output management: PIECES will not just produce scientific publications but also an evidence-informed community-driven PCP implementation tool supported by technology. The access to such piece of software (including the repositories of EBPs and implementation practices) will be given right away after it is fully developed by M12. The idea behind this is that other stakeholders (including other projects funded under this same call) can start benefiting from the tooling as early as possible; c) Measures to ensure reproducibility of research outputs: following the FAIR principles for responsible management of research data, the datasets collected in the project will be published in domain-specific data sharing repositories to ensure other researchers can take advantage of them; d) Involvement of relevant knowledge actors including citizens, civil society, and end-users in the co-creation of R&I agendas and contents: the WP6 Stakeholder and expert participation will warrant the involvement of all stakeholders and consideration of their perspective, open science practices.

4.5. 4P-CAN

Employing an innovative approach, 4P-CAN endeavours to unravel the intricate interplay of factors surrounding individuals, elucidating how these factors contribute to cancer risk across macro (national), meso/mezzo (community), and micro (individual) levels. Aligned with the recommendations outlined in the European Code Against Cancer, 4P-CAN integrates diverse scientific domains, including implementation research encompassing economic sciences, social sciences, and humanities (SSH), behavioural sciences, and cutting-edge social networks methodologies. This interdisciplinary fusion lays the groundwork for the development of novel, personalised tools tailored for cancer primary prevention within Central and Eastern European countries.

4.5.1. Understanding Individual Behaviour

At the core of cancer primary prevention lies the need to understand and influence individual behaviours that contribute to cancer risk. 4P-CAN conducts extensive research to analyse attitudes, motivations, and behaviours related to cancer prevention measures, such as smoking cessation, healthy diet, physical activity, and vaccination. By gaining insights into the factors influencing individual choices, the project aims to develop targeted interventions that promote healthy behaviours and mitigate risk factors. This is achieved through the work in two Living-labs (WP5), in Romania and Bulgaria, with the latter also focussing on environmental factors, such as Radon exposure.

4.5.2. Leveraging Behavioural Insights for Intervention Design

4P-CAN integrates insights from behavioural science into the design of prevention interventions in the Living-labs. By understanding the cognitive biases, social norms, and environmental cues that influence behaviour, the project develops interventions that are more effective in promoting sustained behaviour change.

Moreover, beyond the Living-labs, 4P-CAN involves the understanding of how to leverage behavioural economics principles, social marketing techniques (in the work package dedicated to WP3 *Socio-economic and informational determinants of cancer prevention*), and persuasive communication strategies to nudge individuals towards healthier choices and lifestyles. More precisely, social norms will be tested among students, with the aim of understanding how peer-influence and the informational space, influences their decision to smoke or quit smoking.

4.5.3. Implementing Effective Communication Strategies

Communication plays a pivotal role in promoting behaviour change and fostering the adoption of preventive measures. 4P-CAN employs innovative communication strategies tailored to diverse populations and contexts. In the work package dedicated to WP4 *Targeted public health communication campaigns*, the 4P-CAN key partners with the guiding of IARC, aim to understand the cancer literacy of people in the Eastern countries of the consortium through a series of national surveys (structured on the main behavioural stages; precontemplation, contemplation, preparation, action, and maintenance), and subsequently create effective communication campaigns, built on the principles of implementation research. This will also guide the 5th edition of the European Code Against Cancer.

4.5.4. Empowering Communities through Participatory Approaches

Community engagement is key to the success of cancer prevention initiatives. 4P-CAN adopts participatory approaches, such as Living Labs and community-based participatory research, to involve traditional and non-traditional stakeholders and communities in co-creating and implementing prevention strategies. By fostering collaboration and ownership at the grassroots level, the project ensures that interventions are culturally relevant, contextually appropriate, and responsive to the needs of local communities. 4P-CAN benefits from Citizens Juries at the Living-labs level (Romania and Bulgaria) and National Standing Committees in all the Eastern European countries involved in the project.

4.5.5. Informing Policy and Practice

The diagnosis phase of 4P-CAN starts with a *Multi-level Assessment of Cancer Risk Factors Preventive Legislation*, where policies and legislation are mapped in the EU Member States, as well as the non-EU countries involved in the project, to better understand the macro context. Stakeholders are also mapped at the national level. Then, through the insights gained from the other work packages mentioned above, the work is summarised in WP6 dedicated to Co-creation of evidence-based Policy recommendations.

By translating research findings into actionable recommendations, the project advocates for policy reforms, resource allocation strategies, and structural changes that support the adoption of preventive measures at the population level. This advocacy is essential for driving systemic changes and creating environments conducive to healthy behaviours and lifestyles.

4.5.6. Digital Primary Prevention

The 4P-CAN project aims to explore the design of an AI algorithm to integrate lifestyle data for calculating cancer risk. This innovative approach holds significant potential for improving accuracy in risk perception, enhancing response efficacy, and increasing participation in cancer screening programs and preventive measures. Advances in information technology, computing, and data science, including artificial intelligence and machine learning, have revolutionized public health by enabling the development of tailored interventions and personalized health monitoring. By leveraging big data and predictive analytics, coupled with wearable physiological sensors and personal health devices, it is possible to monitor health behaviours and outcomes more effectively.

However, in many Central and Eastern European (CEE) countries, targeted interventions utilizing such technologies are not feasible due to the absence of necessary technology systems and data. To address this gap and accelerate progress in cancer prevention, the 4P-CAN project proposes harnessing alternative sources of data, particularly focusing on individuals' attitudes, perceptions, and behaviours.

The 4P-CANcer algorithm design seeks to integrate a wide range of data sources, including individual self-reporting on factors such as age, sex, comorbidities, socio-economic status, lifestyle habits (e.g., physical activity, smoking, alcohol consumption), vaccination status, and environmental factors. This data is merged with national and regional datasets on socio-economic indicators, political determinants of health, and environmental pollution.

Another Digital dimension in the project is the creation of interactive Country Dashboards that will integrate the cancer risk factors mapped through the project, in national dashboards summarising the cancer primary prevention situation in each Eastern European country of the consortium.

4.6. PREVENT

In PREVENT a multi-domain approach is adopted, particularly at individual, family & peers, childcare & school, society and public policy domain. Several biological, socio-economic, and environmental factors interact together, at each domain level, to prevent from a large-scale implementation of the current primary interventions planned for a weight control management during childhood and adolescence. PREVENT proposes a multi-actor and context aware primary intervention approach, along with specific engagement policies and educational plans, with the main aim at addressing these barriers.

4.6.1. Communities of Practice - CoPs

For this purpose, Communities of Practices will be created of a multi-discipline composition, one CoP per pilot case of PREVENT. Their role is to monitor, supervise, advise, and modify the research implementation processes of PREVENT ranging from the identification of the barriers in implementing existing intervention policies, especially at large-scale, to the proposal of the new PREVENT intervention/engagement strategies, addressing the current barriers, along with the respective actions for upscaling.

4.6.2. Health Policies

Healthcare professionals of different specialties (e.g., pediatrists, psychologists, psychiatrists, nutritionists, etc.) are involved in each of the three PREVENT pilots (Greece, Sweden, Spain-Catalonia). In addition, PREVENT includes three health associations in cancer, obesity, and health management (EHMA, EASO and CPE), horizontally acting for all pilots. PREVENT sets scientific target to specify the childhood medical indicators that relate obesity with cancer risk in the adulthood, also relating with other co-morbidities and clinical risk factors, and order them with respect to their significance for carcinogenesis. Meta-analysis is carried out by surveying existing clinical studies and trials to quantify and clarify the role of clinical and socio-economic factors on childhood obesity and cancer risk. Healthcare professionals in PREVENT and CoPs actively involved in dedicated engagement actions to bring the evidence-based information before children, their families and peers, teachers and educators to maximize the impact of weight control management policies thus cancer prevention.

4.6.3. Social Impact

PREVENT proposes new multi-actor and context-aware primary interventions accompanied with engagement strategies to prevent obesity and overweight during childhood and adolescence which is proven by evidence from clinical studies that increase cancer risk in the adulthood. The PREVENT interventions are multi-actor in the sense they design to target all different types of users within the school community. PREVENT targets children/adolescents of age (9–16-year-old), family/guardians and peers, teachers/educators, food school suppliers and PA experts. Additionally, the project LLs will be designed and setup in a way to target citizens of different profiles, such as economic status (poor/rich/medium), regional characteristics (urban, rural), social factors (one parent family, family of many children, family issues), medical & biological factors (co-morbidities, family history on obesity and cancer), cultural attributes (the cultural environment, religion), and local food attributes (near sea-fish consumption, in the mountains-meat consumption). Moreover, in PREVENT, as gender we do not only refer to the epidemiology considerations of the biological aspects between male and female (e.g., the

"sex" dimension) but also the "sociological" attributes affecting the development and progression of obesity and overweighting during childhood and adolescence.

4.6.4. Digital Engagement Means

a)   the AR and gamification app: PREVENT will adopt culturally aware games delivering Computerized Cognitive Behaviour for promoting healthy habits to prevent obesity. PREVENT will deliver natural and believable interaction and empathic virtual coach supporting end-users in healthy habits management and monitoring. An example of this type of solutions could be the development of a character in AR, this character could be linked to the chatbot, with STT speech-to-text, TTS text-to-speech, and lip-sync modules. User will have the feeling of talking to the character as if he/she was talking to a real person.

b)   Virtual assistance: PREVENT will exploit recent advances in natural language processing and chatbot technology to deploy and demonstrate a virtual health and fitness assistant that will support routine and behaviour change of users towards healthier lifestyles. In order to motivate users to adopt healthier choices to support a healthy and balanced diet and lifestyle, the virtual health and fitness assistant, in addition to delivering content adjusted to the specific target groups, will provide a wide range of features including: a) enabling setting of health/fitness goals and progress monitoring, b) sending motivational messages regarding the user's health and fitness plan, c) helping the users to keep track of their workouts, sleep quality and health data, enabling also comparisons between different periods, d) responding to inquiries e.g. about suggested activities, and e) receiving user's feedback (e.g. through questionnaires). The interface of the chatbot will be available in users' native languages.

c) The mobile front-end digital engagement platform (questionnaires, interviews, feedback): PREVENT will provide a lifestyle app that will enable young users to manage their own wellness and develop increased awareness on obesity aspects (linked with certain lifestyle risk factors). The application will utilize gamification elements in order to increase the user engagement and will enable the monitoring/reporting on certain lifestyle aspects (e.g., diet, physical activity, mental/stress state). The service is currently available both in Android and Apple devices as well as through a (responsive) web-UI. The service is GDPR compliant and supports the most popular wearables (e.g. Apple Watch, Garmin, Fitbit etc.) currently in market.

d)   Geo-environmental analysis platform: PREVENT will deploy an external analysis tool to enable student driven reporting about their individual living environment parameters (e.g., built environment and foodscape), relevant to lifestyle habits (e.g., own reports of food availability in their immediate living environment, reporting of exposure to food promoting material, reporting of frequently visited food retailers etc.). The independent platform, handling picture-based and report-based data collection from children, has been developed together with secondary education students and teachers, to support population monitoring on the level of ecological parameters known for affecting dietary and physical activity behaviors within these populations.

4.6.5. Trustworthy AI for data analysis

A school-centric setup of the LL, considering local socioeconomical, geo-environmental and functional school requirements will be established in each eco-system (Catalonia-Spain, Greece, Sweden). Moreover, PREVENT will implement concrete measures to address the well-established childhood/adolescence obesity or overweighting sex and socio-economic differences, integrating gender dimension into its implementation research framework. PREVENT will develop an Analytics Framework for the collection, storage, harmonization, curation, anonymization, and analysis of the data collected during the implementation of the LL. Interpretable, explainable, and trustworthy AI will be incorporated to transform the raw data into interpretable features from which valuable information can be retrieved that will enable the evidence-based policymaking of the project.

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4.6.6. The Active Behavioural Change Model

In PREVENT, an active behavioural change model is adopted, and it will be adapted to the needs of the PREVENT LLs methodology. The model is based on the principles of the transtheoretical theory (TTM) of behavioural of change, which describes five main behavioural stages; precontemplation, contemplation, preparation, action, and maintenance. The goal of the theory is to avoid recession into the relapse stage when the trained behaviours relapse into a pre-training state. Following the basic active behavioural of change model principles and the respective processes of change, PREVENT investigates specific implementation research methods as to how these theories can be brought implemented (self-reports, digital means, motivational interviewing, targeted education, self-evaluation & user empowerment).

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5. Common Cluster R&I Activities between the projects

In Table 2, cross-cutting scientific domains between the cluster projects are presented. For each and all of the cross-cutting areas, the management teams of the cluster projects will proceed with a series of actions, as presented below.

1. *Table 2 Cross-cutting domains*

SCIENTIFIC DOMAINS	CO-CAPTAIN	CPW	ONCODIR	PIECES	4P-CAN	PREVENT
Communities of Practice – Stakeholders Groups				√		√
Co-creation and Living Labs	√		√	√	√	√
Health Policies	√	√	√	√	√	√
Health inequalities	√	√	√	√	√	
Health Economics		√	√			
Social Innovation	√	√	√	√	√	√
Behavioural Change Model	√	√	√	√	√	√
Digital engagement means		√	√	√	√	√
Artificial Intelligence (AI)			√			√

Distribution of Activity Responsibilities: Assigning specific roles and tasks per Scientific Domain (as presented in Table 2) to different projects ensures a balanced distribution of workload and leverages the unique strengths and expertise of each project team. This structured approach enhances efficiency and effectiveness in achieving the cluster's objectives.

Citizen's and end user's requirements exchange: The success of any project hinges significantly on the meticulous elicitation and definition of user requirements. During the definition of user requirements co-ideation and co-creation, knowledge sharing, and experience exchange play pivotal roles, particularly when adhering methodologies like design thinking. However, given the diverse scopes, cancer types, technical maturity levels, and unique needs of each project, it becomes crucial during cluster activities and Living Labs to pinpoint commonalities and approaches that facilitate a more holistic approach to addressing challenges. While some projects may have already identified an initial set of user requirements, it is imperative to embrace an iterative process that enhances citizen and end-user engagement in co-creation and co-design activities. Despite potential constraints such as budget, time, or technical limitations, these activities serve as catalysts in identifying opportunities for future collaborations and provide insights on certain (relevant) aspects that can or should be addressed by one project and can be shared to the other (e.g., AI or ML based tools for decision making for effective prevention of cancer).

Joint cluster workshops: Workshops that bring together professionals from various disciplines and different projects create an environment where diverse perspectives and methods can be shared. This approach leads to a more comprehensive understanding and prevention of Cancer, Such a holistic view is essential for developing effective strategies for prevention. Networking opportunities, provided by these collaborative events, are equally important. Forming professional relationships that may evolve into future collaborations and resource sharing. Through this activity and the facilitation of EC it builds a dedicated community of researchers, clinicians, and other stakeholders, ensuring a continuous exchange of ideas and support. When diverse minds from different disciplines converge, the potential for innovative ideas and solutions is greatly enhanced. This is particularly important in addressing the multifaceted challenges in cancer prevention, which often require insights from multiple fields. Creativity the collective expertise and creativity of a varied group leads to uncovering solutions that may not be evident within a single discipline, paving the way for breakthroughs in Cancer prevention. All projects could

develop educational resources tailored to their unique scope, focusing on specific topics or issues. These resources will be made available through both online activities and in-person events, ensuring a versatile and accessible approach to education. Ultimately, and since primary prevention is our main target, the outcomes and finding of these should be communicated to the society.

Annual Meeting Organization: The organization of annual meetings is a key task that facilitates face-to-face interactions, fostering stronger relationships and collaborations among the cluster partners. Discussing the organization of these meetings, including the potential combination with meetings at project level, is a strategic approach to maximize resource utilization (i.e. time, financial, human resources) and enhance networking opportunities.

Common white paper for policy recommendations: As soon as the main outcomes of the cluster project become available—alongside supporting deliverables and potential scientific publications—the discussion for policy recommendations will be initiated. At this stage, a key topic on the agenda of cluster meetings will be deciding whether to develop a common white paper containing key policy recommendations or a more comprehensive policy brief. Cluster projects are encouraged to align some of their recommendations, proposing specific changes related to the cancer types they address. This collaborative approach adds value to the recommendations and helps policymakers review a cohesive set of recommendations covering various cancer types, rather than disparate policy documents from different projects. These recommendations can be tailored to address the specific challenges that every country has based on their status and future trends as indicated in ECIS. Additionally, the Cluster project are particularly interested in organizing focused workshops with experts, EU representatives from HaDEA, and relevant national policymakers. The main goal of these workshops is to discuss the cluster's suggestions and how their adoption could significantly impact the quality of life (QoL) of EU citizens.

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6. Conclusions and Next Steps

The work plan outlined in the preceding chapters has detailed the activities identified thus far at both the project and cluster levels. It will remain a dynamic document, continuously evolving to incorporate any future activities aligning with the common goal of enhancing the Quality of Life (QoL) for EU citizens in line with the Mission Cancer. Numerous potential synergies have already been identified and analyzed, laying the groundwork for forthcoming discussions and collaborations that will amplify the impact of each project. The progress, results, and outcomes of the upcoming steps will be documented in forthcoming deliverables and/or potential shared documentation.

Subsequent cluster meetings will play a pivotal role in further refining the common strategy, ensuring ongoing engagement with experts, EU representatives, and relevant stakeholders. This iterative approach aims to foster continuous improvement and alignment with the overarching mission.

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