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Centre for Innovation in Medicine

Contribution to the European Commission Call for Evidence regarding Council Recommendation on cancer screening

(22nd of February, 2022)

Key Recommendations:

- to include the **social innovation** in the screening programs design
- to take into consideration the **site agnostic testing** for screening
- to include **real-time real-world data**, digital-enabled screening

Background

Centre for Innovation in Medicine, an European research & innovation civil society organization, with interest in innovative health policies and health education and personalised communication, welcomes the invitation of the European Commission to contribute to the public consultation on the update and possible extension of the 2003 Council Recommendation on cancer screening.

The inequalities in cancer screening are a known reality in the EU

"*It shouldn't matter where you're born and where you live. (...) A woman with cervical cancer who lives in Romania is 16 times more likely to die than a woman who lives in Italy*" - President Ursula von der Leyen during the launch of the public consultation for Europe's Beating Cancer Plan (February 2020)(1).

> *"We have come a long way, but we still face differences between Member States. A recent Eurostat study showed that in one Member State, 62% of women between the ages of 50 and 69 have had mammograms in the last two years, while in another state the percentage is 0.2%. This is a huge difference and it is inadmissible in the Europe of the present" - Commissioner Stella Kyriakides (February 2020).*

The failure of screening programmes requires new types of actions

Romania has the highest rate of mortality by cervical cancer in the European Union. Every year, in Romania, there are 1,800 deaths from cervical cancer and 3,400 new cases. At European level, Romania ranks first in terms of incidence and mortality: the incidence is 2.5 times higher than the European average, and the mortality rate is over 4 times higher(2).

In 2017, a woman in Romania was diagnosed with breast cancer every hour; every 3 hours, a woman died of breast cancer; and half of the women diagnosed were under the age of 60(3). While the European annual mortality rate for breast cancer in Europe is 26%, the same rate in Romania reaches 35%.

In **2012**, Romania launched its **first cervical cancer screening programme**, targeting approximately 6 million women aged 25-63 years (in a period of 5 years). **By 2015, only 7% of the target population was tested**(4).

In **2018**, Romania launched its **first breast cancer screening pilot programme**(5). However, according to the latest Eurostat survey, **only 9% of women in Romania aged between 50 and 69 reported in 2019 that they had a mammogram in the last 2 years**. Once again, Romania ranks last in the EU. For Bulgaria, which is in the penultimate place, the percentage is 36%. In Sweden, the percentage is 95%, about 11 times higher(6).

Fatalism - a great unaddressed barrier in accessing screening programmes

The Centre for Innovation in Medicine measured the attitudes, perceptions and behaviors in the Romanian population every two years starting with 2016. In 2020, 78% of the Romanians that participated in the study believed that cancer can be prevented, compared to 82% (in 2016, 2018). This belief was rather present in the segment that had no experience with the disease. Over 80% of respondents believed that the disease can be detected in early stages. Data are divergent: a large majority of the population is aware that there are cancers which can be prevented and early diagnosed, but just a small minority in fact joined the screening programs (for cervical and breast cancer), defining the failure of screening programs to convert the positive awareness into preventive health actions.

More than 70% of the people questioned said that there are cancers that can be cured, but when asked if a cancer diagnosis always leads to death, more than 45% agreed. This indicates **fatalism**, a condition in which many citizens try to cope with the prospect of cancer, considering that the health system, for various reasons, cannot provide them with the care they need (including cancer screening).

Measuring fatalism in relation to cancer is important because it can indicate people's willingness to take action in all the areas of cancer continuum, including to participate in screening programs, to adopt preventive measures and to access precision diagnosis and innovative therapeutic options.

In this context, the Centre for Innovation in Medicine recommends to the European Commission and the EU Council to include advances in social innovation, cancer screening innovation and digital innovation in order to close the inequalities gap.

Social innovation: behavioral determinants of cancer screening

Despite the high percentage of people that believe that cancer can be prevented and cured, Romania has the lowest screening rates in the EU for cervical and breast cancer (the only types of cancer screening implemented so far).

It's clear that in order to use innovation for reducing inequalities in cancer cancer and more importantly, in cancer screening, the adoption of social innovation measures is needed. The first and most important point to be underlined is that **cancer care (incl. screening) can no longer be patient centric, but citizen centric**, because:

- all patients are first of all citizens and the majority of the citizens will be at some point patients or carers, with a certain percent of them being cancer patients;
- half of the initiatives in the cancer continuum - prevention, screening and palliative care - address actually a citizen, before or after he becomes a cancer patient.

Screening programs should be implemented in a citizen-centric model, moving from the current patient, doctor or health systems centric models.

The citizen-centric model for cancer screening requires a deep understanding of attitudes, perceptions and behavior of the citizens, at macro, meso and micro level, as the foundation for successful screening programs. The macro level refers to the assessment of the influencers of the health behavior that currently are on traditional mainstream or social media; meso level require the assessment of the influencers of the health behavior from the community (religious leaders, professors, mayors etc); micro level include the inner circle of every citizens (close family, very close friends, some medical doctors - family doctors or doctors treating chronic conditions for many years).

The assessment of the individual behavior and key healt influencers should be followed by personalised communication and engagement campaigns, moving away from the standard one-size-fits-all communication and engagement activities that are part of the current cancer screening activities.

There is a vicious circle going on in CEE countries with regards to cancer screening - the more the people do not access the already existing minimal screening programmes, the less these programmes are financed the next year. The first step in addressing the inequalities in accessing cancer screening is to increase adherence to the already existing programmes by personalized communication and actions.

Cancer innovation: the way to site-agnostic screening programmes

While it is important to launch screening programmes for as many types of cancer as possible, these efforts must take into consideration that the cancer understanding has evolved in the last years and it can no longer be classified only by the organ location of the primary tumor, but by taking into consideration the molecular characteristics of the disease.

Cancer screening means looking for cancer before symptoms appear, when cancer may be easier to treat. A recent study shows that identifying all solid cancers before they metastasize could prevent more than 20% of cancer deaths within 10 years of diagnosis and highlights the importance of cancer screening and early detection in cancer control (*one of the studies that actually quantifies the contribution of screening in cancer control)*(7).

With cancer therapeutics we have witnessed a revolution with site-agnostic indications, where a biomarker or group of biomarkers defines the disease and selects the eligible populations regardless of organ or tissue.

Most of the standard screening tests (mammography, X rays, CT scans, even PAP smears) are designed to detect the presence of tumors by assessing their anatomical site at the macroscopic or microscopic levels (looking at cells from the tissue where changes are expected). At present, **research is more focused on the development of minimally invasive or noninvasive biomarkers that can complement traditional tools to better capture the cancer continuum and identify the transition towards pre-malignant states.**

Genomics, transcriptomics, epigenomics and other emerging omic disciplines are changing paradigms in oncology, providing noninvasive molecular assays that go beyond tissues to trace early markers of cancer. **An increasing number of studies show that noninvasive molecular markers combined with diagnostic imaging can provide better strategies to cancer screening**(8)**.**

Understanding cancer biology has prompted researchers to look into more detail for early indicators of disease in products shed by the tumor or generated by the host. **New types of molecules such as non-coding RNAs** have been reported as promising markers for the screening of common types of cancers: lung cancer(9), breast cancer(10), colorectal cancer(11), gastric cancer(12).

Such data proves that molecular assays based on multiomic analysis are becoming high-quality triage tools, selecting patients who require further anatomical investigation. Moreover, these are convenient and safe and are likely to increase screening coverage in the general population and make repeated testing practical and affordable.

The complex nature of forecasting disease risk has also been taken to another level **by artificial intelligence**. Recently, the UK introduced a world premiere in the healthcare system: a test that determines cell-free DNA and uses AI algorithms to rule the most common cancers, including breast, gynaecological, skin and head and neck cancers(13).

Another innovative approach recently published in Nature shows that by analyzing epigenetic markers from pap smears it is possible to monitor women at risk of breast cancer(14) and ovarian cancer(15). These are the first steps towards developing a better screening tool for four cancers (cervical, breast, ovarian, endometrial cancers) using a single sample collected during cervical screening.

Researchers from the University of Oxford also propose that metabolomic testing can offer a quick way to triage patients with non-specific signs and symptoms, allowing doctors to prioritise those patients who require more invasive investigations(16).

As new types of screening tools emerge that provide either alternatives to current methods or complement current methods, citizens must be informed of the choices they have, as well as the advantages and disadvantages of each method. Moreover, some steps of screening programmes could even be taken at home (eg. self sampling for HPV(17), multi-target stool DNA testing for colorectal cancer(18)), increasing adherence to screening by addressing current barriers (distance, cultural factors, stigmatization).

Digital innovation: real-time, real-world cancer screening

Digital tools like apps, EHRs, registries, AI and machine learning or digital twins should be incorporated in the new screening programs design, in different phases and for different purposes. In the digital age, it's the right of every citizen to benefit from all evidence-based technologies for early identification of the risk for cancer(19). The implementation of the above mentioned digital technologies should avoid the digital divide especially for the citizens living in Member States with low levels of health systems digitalisation. Emerging technologies such as AI, machine learning and digital twins can be of particular importance if they are implemented for the real-time screening of EHRs(20) in an attempt to identify early warning signs of cancer based on real-world data.

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