

# The Value of Diagnostic Information (VODI) in Cancer care

Policy recommendations for a better future for cancer diagnostics in Europe



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## **Executive summary**

The global burden of cancer is increasing faster than ever and given the impact of COVID-19 on cancer services, it is now crucial that the full potential of laboratory diagnostics for cancer is realised. Laboratory diagnostics play a vital role in prevention (when 30-50% of cancers could be prevented<sup>1</sup>) and in achieving better patient outcomes. In clinical decision making, laboratory diagnostics account for up to 66% of decisions – and yet less than 2% of total healthcare spending is allocated to this technology<sup>60</sup>. **European Union Member States need strong, coordinated policies that recognise the strength of robust cancer screening strategies and early detection. These policies must take a holistic approach** – reflecting the value of diagnostic information across the full cancer care continuum (screening, diagnosis, treatment and monitoring) and for all stakeholders (patients, healthcare professionals, healthcare providers and the healthcare system as a whole).

# Recommendations concerning the implementation of the Europe's Beating Cancer Plan (EBCP):

- 1. <u>National cancer plans</u>: There is an array of actions that the EU can take to promote more robust national policies for prevention, screening and early diagnosis, with a focus on improved programmes, guidelines, infrastructures and awareness.
- <u>Cancer inequalities</u>: Reduce cancer inequalities by assessing country performance in screening and early detection through the Cancer Inequality registries by ensuring that the used indicators include the rate of participation in cancer screening, the time to diagnosis, and the rate of early detection as well as the related enabling infrastructures.

## **Recommendations concerning the general organisation of healthcare systems:**

- 3) <u>Patient access</u>: The **EU needs to enable broad and timely patient access to innovative diagnostics to improve cancer patient outcomes**. Access to diagnostics allows for the most appropriate and personalised treatment for cancer patients, improving outcomes. This can be achieved by providing accelerated and permanent reimbursement of diagnostic tools and adopting EU-wide guidelines to ensure predictability and consistency across Member States.
- 4) <u>Value assessment</u>: When assessing the value of laboratory diagnostics, the assessment methodology needs to be adapted to consider the value of testing for screening and early detection, the clinical value at each stage of the cancer care continuum, and the overall value for society from more people living longer and better quality lives, either in remission or living with cancer.
- 5) <u>Healthcare systems preparedness</u>: Actions must be taken to **improve the preparedness** and continuity of cancer care during future health crises by deploying funds for screening, modernising relevant infrastructures, and a targeted approach to citizens, ensuring healthcare systems resilience. Furthermore, targeted actions need to be taken at the EU level to address the COVID-19 backlog, and **tackle delayed or undiagnosed cancers**.

The paper "The Value of Diagnostic Information (VODI) in Cancer care" provides more information on the value of laboratory diagnostics across the whole cancer continuum, the current situation in Europe and how the above recommendations could be implemented in practice.

# Scope: laboratory diagnostics in cancer care

Laboratory diagnostics can provide critical information at every step of the cancer care pathway, from prevention, screening, and diagnosis to monitoring the progression of a disease, and predicting treatment responses. This paper outlines the role of laboratory diagnostics across the cancer care continuum, the reality they face in Europe, and how a targeted EU effort can increase access to these essential tools.

To diagnose medical conditions and to guide the decisions on the best treatment for patients, healthcare professionals benefit from and count on a range of medical technologies, among which are In-vitro diagnostic (IVD) medical technologies (or "laboratory diagnostics"). As per the World Health Organization, "In vitro simply means 'in glass', meaning these tests are typically conducted in test tubes and similar equipment, as opposed to in vivo tests, which are conducted in the body itself."<sup>2</sup> These are non-invasive tests used on samples from the human body (e.g., blood, urine, or tissues) to determine the status of a person's health (e.g., biomarker and biopsy tests for cancer, automated analysers etc.). Their value resides in the quality of information they provide, which is timely, precise, and patient-specific.<sup>3</sup>

In this paper, the other category of diagnostic technologies, diagnostic imaging (X-ray, CT scans, MRIs, ultrasounds etc.), will not be discussed. This purposeful omission is to achieve a consistent and homogenous picture of the landscape of cancer laboratory diagnostic technologies, which have different functions and market access outlooks.

# I. The value of diagnostic information in cancer care

## A growing burden of cancer in Europe

Every year in Europe, **3.7 million people are diagnosed with cancer, and 1.9 million people lose their lives to cancer**.<sup>4</sup> Cancer accounts for **20% of losses of life in the European region**, contributing to one-quarter of the global total of cases.<sup>3</sup> Due to multiple factors, including an ageing population, cancer mortality is set to increase by more than 24% by 2035, making it the leading cause of loss of life in the EU.<sup>5</sup> Breast and lung cancer are the most common causes of cancer death mortality among women, whereas lung and colorectal cancer are the most common causes among men.<sup>6</sup>

EU citizens within and among Member States face vast inequalities in cancer prevention, detection, treatment, and care, resulting in **disproportionate survival rates across EU countries**, notably survival rates vary by 20% between member states following treatment for breast cancer.<sup>7</sup> In addition, coverage of the target population (determined by age and gender) ranges from about 25% to 80% for cervical cancer screening.<sup>8</sup>

## The impact of the COVID-19 pandemic

The **COVID-19 pandemic has exacerbated existing inequalities and has caused severe disruptions in the cancer care continuum**. Nearly 100 million cancer screenings were not performed in Europe due to the disruption caused by the pandemic. Between 2019 and 2022, cancer diagnoses in Belgium, Italy and Spain fell by over 40%, and there was still a 44% backlog in cancer screening globally by the second half of 2021.<sup>9</sup> This disruption means that nearly one million cancer patients could be undiagnosed, and 1 out of 5 cancer patients have faced treatment delays.<sup>10</sup> The impact of this backlog is expected to be long-lasting, potentially leading to excess mortality from cancer.<sup>11</sup>

## The essential role of laboratory diagnostics in cancer care

Early detection, through screening of asymptomatic populations, and early diagnosis and risk assessment of symptomatic patients can lead to better chances for successful treatment, improved patient outcomes and quality of life, higher chances of survival, and less burdensome care for the individual, their family, and the healthcare systems.<sup>12</sup> Notably, if cervical cancer is detected early, a patient's survival rate would be 92%, but only about 44% of people with cervical cancer are diagnosed at an early stage. If cervical cancer has spread to surrounding tissues or organs, the five-year survival rate is 58%, and if it has spread to a distant part of the body, the five-year survival rate is 18%.<sup>13</sup> Early cancer detection, before any symptom appears, implies shortened duration of treatment and more effective treatment, with a higher chance of recovery.<sup>14</sup> In addition, as early screening might lead to more cases being treated by less invasive procedures, this can improve the patients' quality of life.<sup>11</sup> 57% of people with lung cancer survive for five years or more when diagnosed at stage I compared with 3% at stage IV.<sup>15</sup>

According to the WHO, **effective strategies for early cancer identification can save lives and reduce personal, societal, and economic costs**. It is estimated that treatment for cancer patients diagnosed early is two to four times less expensive than treatment at more advanced stages.<sup>16</sup> An NHS report estimated that the cost of treatment for stage 3 and 4 colon, rectal, lung and ovarian cancer was nearly two and a half times the amount spent on early-stage treatments (i.e. stage 1 and 2).<sup>17</sup> Indeed, the annual healthcare costs are estimated to be  $\in$ 23,280 greater for patients with advanced versus early-stage breast cancer.<sup>18</sup> Indirect and societal costs borne by patients and caregivers (e.g. work-related and home productivity losses) make the difference even more significant.<sup>19</sup>

Laboratory diagnostics play an active role throughout the cancer care pathway, providing key data for screening, diagnosis, treatment, and surveillance.<sup>20</sup> Furthermore, access to screening programs can reduce health disparities, a persistent issue within and across the EU.<sup>21</sup> For example, laboratory diagnostics tests like biomarkers and companion diagnostics can provide the necessary information to make clinical decisions on using targeted treatments for cancer following diagnosis. Therefore, access to diagnostic solutions determines a patient's access to appropriate, innovative or targeted therapies, which have revolutionised the treatment of many cancers and can potentially be lifesaving.<sup>22</sup>

# The value of diagnostic information in breast, cervical, lung and colorectal cancers

While diagnostic information is valued differently by various stakeholders, cancer screening and early detection hold benefits for all: patients, healthcare professionals, the healthcare providers and the healthcare systems as a whole<sup>1</sup>.

#### **Patients**

- Increased survival rates and life expectancy<sup>24,25</sup>
- Quality of life improvement:
  - Personalized care<sup>26</sup>
  - Reduced referrals and overtreatment<sup>27</sup>
  - Less invasive diagnostic tests<sup>28</sup>
  - Limited interruption and continuity of employment and return to society of early diagnosed patients<sup>29</sup> and, consequently, caretakers
  - $\bullet$  Reduced burden and informal costs for caretakers and families  $^{\scriptscriptstyle 30}$

#### • Value of knowing:

- Precision of prognosis<sup>31</sup>
- Observe the risk of recurrence<sup>32</sup>
- Reducing psychological burden of false positives<sup>33</sup>

#### **Healthcare providers**

- Pathology laboratory workload reduction<sup>39</sup>
- Reduced costs from false-positive results<sup>40</sup>
- Decreased use of imaging and invasive diagnostic solutions<sup>28</sup>
- Decreased use of treatments like chemo and radiography<sup>41</sup>

#### **Healthcare systems**

- General cost-saving from pathway efficiencies<sup>42</sup>
- Reduced adverse effects (e.g. unnecessary treatment or invasive diagnosis, undetected cancer-associated complications or risks, false positives or false negatives etc.) by greater acceptance of screening<sup>43</sup>
- Cost-saving from avoiding adverse events44
- Cost-effective implementation of new and shorter treatments by predicting response<sup>45</sup>
- Reduced amount of population living with long-term cancer by earlier detection<sup>46</sup>

#### Healthcare professionals

- Improved accuracy & timeliness of decision-making<sup>34</sup>
- $\bullet$  Earlier intervention leading to better outcomes and reduced secondary risks  $^{\rm 35}$
- Reduced unnecessary referral and overtreatment<sup>36</sup>
- $\bullet$  Personalisation of treatment and care and targeted therapy selection  $^{\rm 37}$
- Recurrence surveillance & detection<sup>38</sup>

Examples of laboratory diagnostic solutions available for breast, cervical, lung and colorectal cancers and their impact on the cancer care continuum:

#### Screening

A female patient who has received regular cervical screening (via HPV testing and cervical cytology/pap test) has a greater chance of learning about precancerous changes in her cervix, often making treatment possible before cervical cancer develops.<sup>47</sup> If this cancer is detected early, her five-year survival rate would be 92%, but only about 44% of people with cervical cancer are diagnosed at an early stage. If cervical cancer has spread to surrounding tissues or organs, the five-year survival rate is 58%, and if it has spread to a distant part of the body, the five-year survival rate is 18%.<sup>48</sup> Therefore, regular screening strategies are lifesaving.

#### Diagnosis

A female patient is newly diagnosed with all-invasive breast cancer. Between 20-30% of women would carry a certain gene that is associated with the growth of breast cancer and that can be identified via a tissue biopsy.49 Depending on the presence or absence of this gene, she would be treated with targeted gene therapy or with standard chemotherapy.<sup>50</sup> It is paramount to make the right diagnosis in order to prescribe the right, least invasive, and least costly treatment. To do that, healthcare professionals (pathologists, oncologists, and surgeons) involved in test interpretation need to be continuously trained on the latest guidelines, while it is ensured that those are consistently updated for the latest testing developments, and also trained on consistent interpretation of test results.<sup>51,52</sup>

#### Treatment

patient with metastatic colorectal cancer should always undergo an assessment of specific gene mutation, which causes cancer's growth. Genotyping of such mutation via tissue and plasma samples has been shown as a viable solution to detect it and can also be used to detect the emergence of mutations during treatment, as well as the treatment's resistance and efficacy in the patient.53 An accurate test for such gene mutation will determine the patient's eligibility for certain targeted therapy. It would also benefit the clinical practice by better informing their decisions to administer treatment independent of cancer tissue availability.54



#### Monitoring

A patient has just completed their lung cancer treatment. However, their care journey has not ended with the active curative treatment. Continuous monitoring and follow-up are necessary, as cancer cells may have remained undetected upon the end of the treatment. The recurrence risk factors include among others (e.g. age, gender, smoking status etc.), the type and stage of cancer was first diagnosed and the types of treatment given.55 Approximately half of the people who undergo lung cancer surgery will have a recurrence within two years, which is more likely for those treated with radiation or chemotherapy.<sup>56</sup> The monitoring can be based on various methods, like liquid biopsy examining the DNA & RNA of the patient via body fluid. Such solutions offer the advantage of reduced exposure to radiation testing and accompanying pain or complications, ease of sampling, and reliable detection of asymptomatic and treatable metastasis, which can lead to a longer survival duration. To have the best patient outcomes, specific recurrence surveillance recommendations and guidelines are necessary to lead to consistent and efficient monitoring of recovered patients.57

Systemic value for healthcare providers and the healthcare system

Appropriate screening programs can be an important factor in cost-saving for healthcare systems. Population screening programs for patients with colorectal cancer are essential to discover the disease in an early latent stage and treat it adequately before it poses a threat to the individual. Screening acts as a method on its own to fight the disease, and studies show a positive balance between investment in specific colorectal cancer screening strategies and the benefits from life-years gained from it.58 Furthermore, breast cancer patients who are screened for gene mutations and receive positive results are typically treated with targeted therapy. Depending on their initial result, they may be prompted to undergo a so-called reflex testing, adding additional accuracy and precision to the diagnosis. This leads to better-targeted treatment and the reduction of investment in unnecessary treatments.<sup>5</sup>

# II. The reality of cancer diagnosis in Europe

The availability of appropriate cancer diagnostics tests is paramout to ensure patient access to personalized cancer treatment, which is currently hindered by the low levels of promotion, acceptance, and application of laboratory diagnostics in Europe.<sup>60</sup>

When it comes to diagnostic testing, Northern and Western European countries tend to invest more than Eastern European, Southern European and Baltic countries.<sup>61</sup> This contributes to an imbalance in health equity in Europe and fragmented access and delays in oncology testing, in particular,<sup>42</sup> as well as proportionate mortality rates.<sup>62</sup> There are discrepancies in the investment in various cancer screenings, too.



As per the latest European Commission (EC) Cancer Inequalities Registry, there are only two metrics looking at the use of laboratory diagnostics – on colorectal and cervical cancers. The results show that the percentage of people (50-74 years old) that self-reported to have never performed colorectal cancer screening using faecal occult blood test was around 49% average in the EU while in some countries, it was as little as 17%. The percentage of women (20-69 years old) who reported to have never had cervical smear test varied from almost 2% to 47%.<sup>63</sup>

According to the latest "IVD Market Statistics Report" of MedTech Europe for 2021, the differences in total healthcare expenditure, both in relative terms to gross domestic product (GDP) and absolute amounts, demonstrate the wide variation in general access to healthcare across the 31 countries in this report. Relative to GDP, Switzerland is the leading country at 13.2%, followed by France, Germany and Norway.<sup>64</sup> At the same time (in 2019), other countries' expenditure was significantly lower, e.g. Bulgaria (7%), Estonia (6%) and Romania (5%).<sup>65</sup>

Public expenditures for better and earlier diagnostic and treatment can reduce cancer-related economic losses.<sup>66,67</sup> Despite the clear economic rationale for investing in better diagnostics, there are still several barriers to exploiting the potential of diagnostics:





# III. A context for action

Recent initiatives, such as Europe's Beating Cancer Plan<sup>8</sup> or the Cancer Mission<sup>68</sup>, and relevant declarations made by the EU Council and the European Parliament confirm a growing recognition of the need to improve and innovate the EU's approach towards cancer. With a focus on prevention, early detection and treatment, **Europe's Beating Cancer Plan creates a unique policy context to recognise the value of testing**. The Plan entails several promising flagships to realise this ambition:

- The update of the 2003 Council Recommendation on cancer screening in 2022 to reflect latest scientific evidence
- The establishment of a Cancer Inequalities Registry
- The new 'Cancer Diagnostic and Treatment for All' initiative, and the 'Genomic for Public Health' project
- The development of a new EU Cancer Screening Scheme
- The 'Partnership on Personalised Medicine'

In addition, the European Parliament has adopted recommendations for a comprehensive and coordinated EU strategy to fight cancer; **asking for quicker access to molecular testing and increased access to advanced sequencing diagnostics** by earmarking financing and creating clear pathways for fast and efficient reimbursement.<sup>7</sup> In fact, the EU4Health Programme, represents a unique opportunity for future funding at the EU level, with the European Commission already allocating  $\in$ 146.9 million for the fight against cancer in 2022.<sup>69</sup>

While implementing the several flagships of its Beating Cancer Plan, **the European Commission could take note of the long-lasting gaps in cancer detection and diagnosis**. These include insufficiencies in the national implementation of cancer screening programs. Notably that 75% of the European cancer cases are not subject to screening, detection and treatment, there is low public awareness of cancer screening programs, low uptake of tests and approaches to early detection and weak referrals.<sup>10</sup>

# IV. Policy recommendations for a better future of cancer diagnostics in Europe

The medical technology industry welcomes the EU-level actions to prioritise cancer care. The steps have the potential to bring cancer care to a new stage that has value for all stakeholders – patients, caretakers, healthcare professionals and providers, the healthcare system, and society. **EU and Member States should act now to progress cancer care to the next stage**. These actions include strengthening and implementing national cancer plans, reducing cancer inequalities around Europe by improving the use of the cancer inequalities registries, improving patient access to screening and early detection, and to appropriate treatment, adapting value assessment methodologies and building better healthcare preparedness for future health crises and eliminating the COVID-19 backlog. **The medical technologies industry would like to propose several recommendations to lead to a better future for cancer diagnostics in Europe**.

# Recommendations concerning the implementation of the Europe's Beating Cancer Plan (EBCP):

## 1) National cancer plans:

Several National Cancer Plans remain incomplete. Eight member states still do not have population-based screening programmes for breast cancer, cervical cancer and colorectal cancer.<sup>70</sup> And for countries, which already have plans in place, there are still possibilities for expansion to additional cancer areas, and greater awareness and training efforts are possible. There are several **actions the EU can take to promote stronger national policies**, with a focus **on improved programmes, guidelines, infrastructures and awareness for prevention, screening and early diagnosis**. The following concrete actions could be recommended for Member States:

- Employ funds, clinical and testing, and patient management guidelines, minimal testing standards and exchange of best practices and methodologies for better implementation of EU recommended cancer screening programmes.
- Extend population-based screening programmes for breast, cervical, lung, colorectal, prostate and gastric cancers, especially where the cost-effectiveness is proven (as per the "Cancer screening in the EU" scientific opinion on the Group of Chief Scientific Advisors to the EC<sup>71</sup>).
- Improve participation of citizens by raising awareness of the public, potentially through EU and national campaigns.
- Enhance training of healthcare professionals to raise awareness on the latest laboratory diagnostics innovations, leading to more accurate and precise diagnosis and quicker referral of the patient to oncology specialists once cancer is detected.
- Allocate permanent and sufficient funding for screening and early detection programs and improve enabling infrastructure (i.e. appropriate resources to provide the necessary capacity for the expected increase in testing volume).

### 2) Cancer inequalities:

Reduce cancer inequalities by assessing country performance in screening and early detection through the Cancer Inequality registries going forward and by ensuring that the used **indicators include the rate of participationin cancer screening, the time to diagnosis, and the rate of early detection as well as the related enabling infrastructures**. In more detail, inequalities can be reduced by addressing the following needs:

- Successful indicators need to assess the participation rate in screening, time to diagnosis, the stage of cancer at the time of diagnosis, and the time of patient referral post-detection.
- The social inequalities indicators need to look for the access of hard-to-reach groups (e.g. people living in remote locations) to cancer early detection and follow-up healthcare services and dedicated strategies need to be implemented to address those gaps.
- Enabling infrastructure for diagnostic testing needs to be assessed, including a sufficient number of analysers and health care personnel to carry out an increased testing volume due to the extension of cancer screening recommendation. This would shed light on where to act to ensure those enabling infrastructures and accompanying human resources are sufficient to reduce cancer inequalities.
- Reimbursement coverage available for screening and early detection needs to be assessed consistently to stimulate action on where access gaps appear in result of missing reimbursement strategies.

## 3) Patient access:

While there is an array of innovative diagnostic tools available, there is considerable underuse of their potential as patients often lack access to them.<sup>63</sup> This is usually because the reimbursement of such solutions and their deployment in healthcare systems varies considerably across Member States. The **EU** needs to work towards better patient outcomes by ensuring that they have broad and timely access to and innovative diagnostics allowing for the most appropriate and personalised treatment. That could be achieved by the following actions:

- The funding and reimbursement of laboratory diagnostic technologies needs to be timely and based on their long-term economic and societal impact.
- The European Commission could establish EU-wide guidelines to better inform national decisions on funding and reimbursement of In-vitro Diagnostics and ensure predictability and consistency in the decision-making process across Member States.

## 4) Value assessment:

Given that diagnostics amount to less than 2% of the total healthcare spending but are relied on for 66% of the clinical decisions, their value needs to be assessed holistically.<sup>72</sup> When determining the value of laboratory diagnostics, the assessment methodology should be adapted to consider:

- The value of testing for screening and early detection for all stakeholders;
- The clinical value at each stage of the cancer care continuum, reflecting the role of prevention, proper treatment, proper use of resources etc;
- The overall value to society from more people living longer and better quality lives, either in remission or living with cancer;

## 5) Healthcare systems preparedness:

Actions must be taken to **improve the preparedness and continuity of cancer care during future health crises** by deploying funds for screening, modernising relevant infrastructures, and a targeted approach to citizens. Furthermore, there are considerable delays and backlog in cancer screening and diagnosis due to the COVID-19 pandemic, which will likely remain an issue for the years to come.<sup>73</sup> Targeted actions need to be taken at the EU level to address this and **tackle delayed or undiagnosed cancers and avoid the enhanced costs of treatments of cancers diagnosed later, increased mortality rates and treatment failure rates**. Those actions, which can address the delays and contribute to future preparedness and continuity of cancer care in times of future crises, should:

- Deploy funds from the EU4Health programme for pan-EU cancer screening and early detection programmes and adopt the latest diagnostic tools, including self-sampling innovative diagnostic methods.
- Support local hospitals, screening and diagnostic facilities (laboratories) and cancer care facilities across member states by modernising their screening and early detection infrastructures and targeted approach to patients.
- Target all citizens, with a special care for groups of citizens that are frequently underserved due to various factors (e.g. remote areas).

# Conclusion

The value of laboratory diagnostics in cancer is undeniable – for individuals, for healthcare systems and for society. While policymakers recognise the urgent need to proportionately address the increasing burden of cancer – through initiatives like the Europe's Beating Cancer Plan – there is still much to be achieved concerning the role of laboratory diagnostics. This paper outlines key recommendations from the medical technologies industry that can support the EU in achieving its mission to beat cancer and supporting healthcare systems to manage cancer more effectively. Acting cohesively and without delay makes it possible to create a better future for cancer diagnostics in Europe, helping to reduce cancer levels and reverse the damage left behind in the wake of the COVID-19 pandemic.

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