



WHITE PAPER SUMMARY

The impact of cancer-related comorbidities on patient treatment, treatment efficacy, survivorship, and quality of life

Cancer-related complications and comorbidities add a highly significant burden on patients across Europe – and are in many cases fatal.^{1, 2,3} Research shows that most cancer patients, even up to almost 90% depending on the cancer type and age, report at least one comorbid condition.^{4,5,6} Patients with comorbidities are at increased risk of complications on anticancer treatments, which can have a detrimental impact on the efficacy of cancer management. On the other hand, both cancer and its treatments may impact on comorbidity outcomes.⁷ Therefore, it is crucial to alleviate the burden of cancer-related comorbidities and complications through a more systematic and routine risk assessment and management, which can reduce the burden of morbidity and mortality associated with complications and comorbidities. Patients with comorbidities are less likely to receive anti-cancer treatment with curative intent.^{8,9} while they have a lower life expectancy and experience an impaired quality of life.¹⁰ Furthermore, comorbidities are negatively associated with multiple indicators of quality of life.¹¹ Some of the most significant complications and comorbidities are briefly presented below:

Cancer and associated thrombosis (CAT)/ venous thromboembolism (VTE)

Cancer-associated thrombosis (CAT) is one of the leading causes of death in cancer patients^{12,13} as it carries a higher risk of recurrence, bleeding and mortality as compared with controls. In the context of the impact of cancer, systemic anticancer therapies, and pre-existing risk factors that may increase the risk of blood clotting, patients with cancer are estimated to have a 2- to 20-fold higher risk of developing venous thromboembolism (VTE) when compared to non-cancer patients.¹⁴ The specific profiles of cancer patients, comorbidities, the use of anticancer treatments, and the cancer progression itself represent a major therapeutic anticoagulant challenge while CAT remains the number one cause of death during chemotherapy and the second-leading cause of all cancer deaths (after disease progression).¹⁵

Cancer and cardiovascular complications

Nowadays, cardiotoxicity produced by cancer therapies is still a major limitation that can significantly affect the clinical benefits and cancer patients' survival and quality of life.^{16,17,18} The increased burden of cancer treatment-related cardiotoxicity is also becoming increasingly prevalent due to the expanding number of cancer survivors, the frequent use of anthracyclines, anti-HER2 therapies and immune checkpoint inhibitors, new antitumour agents with potential cardiotoxic effects, and treatments combinations.^{19,20}

Finally, the clinical problem “competing risks” between treatments for different diseases such as cancer and the co-existence of comorbidities is a reality often faced in onco-cardiology. This problem raises ethical questions that future research should stress.

Cancer and nutritional support

It is estimated that the deaths of 10-20% of patients with cancer can be attributed to malnutrition rather than to the malignancy itself.² Yet, recent studies in European hospitals found that only 30%-60% of patients with cancer who were at risk of malnutrition

received nutritional support.²¹ Evidence from the existing literature^{22,23,24,25,26,27,28,29,30,31} shows that oncologists and patients are often unaware of cancer-related malnutrition and its impact on oncologic and anticancer treatment outcomes and survival. Evidence also supports the association between nutritional status and chemotherapy toxicity^{32,33} and completion^{34,35,36,37,38,39} while more postoperative complications (particularly wound infections), were recorded in patients with increased risk of malnourishment.^{40,41,42,43,44,45,46}

Cancer and obesity

Recent literature supports that treating cancer with surgery, surgical recovery and outcomes are more challenging and can worsen the condition of obese cancer patients.⁴⁷ In addition, a large number of obese cancer patients receive limited dosages of chemotherapy as oncologists often worry about the treatment toxicity.⁴⁸ Results from studies on obese cancer patients and radiotherapy indicated a link between obesity and inferior outcomes,⁴⁹ increased treatment-related toxicities,⁵⁰ and increased risk of acute late dermatitis.^{51,52} Cancer patients after treatment are often experiencing reduced quality of life, including functional impairment, psychosocial distress, limitations in social functioning, and emotional problems.⁵³

Cancer and mental health

Cancer diagnosis and treatment does not have an impact only on patients' body but also their psychological health. The type of therapy (i.e., surgery, chemotherapy, radiotherapy, etc.) also have an impact on a patient's psychology due to physical changes such as amputations, hair loss, etc., or the concurrent symptoms such as fatigue, pain, nausea, etc.⁵⁴. The presence of mental disorders is associated with a higher rate of all-cause^{55,56,57} or cancer-specific^{58,59,60,61} mortality which appears to be stronger in the case of early-stage cancers.⁶² In addition, anxiety, and depression might result in decreased adherence to treatment, poorer cancer survival, increased suicide risk, and additional health expenditures.⁶³

Cancer and neuro(-psycho)logical complications

Cognitive impairment in cancer patients is frequently observed both during treatment and survivorship.^{64,65,66,67} Cancer patients with brain tumours can develop cognitive impairments related to their attention, memory, and executive function.^{68,69} Cancer-related cognitive changes and impairment also have been documented in patients with non-central nervous system (non-CNS) cancer before the treatment, including verbal memory, language, visual-spatial skills, executive function, and psychomotor function.^{70,71,72} Chemotherapy, either alone or in combination with endocrine therapy, may have an impact on the cognitive status of patients from several cancer types⁷³ while patients under radiation treatment to the brain have been reported to experience fatigue and headaches, as well as cognitive impairment.⁷⁴

Cancer and pain

Pain is the most common symptom of cancer at diagnosis and rises in prevalence throughout and beyond cancer treatment. Persistent cancer pain can, in some individuals,

lead to the development of widespread chronic pain.⁷⁵ Pain during cancer treatment is associated with the stage of the disease and the location of the cancer^{76,77} while increased pain is also associated with specific cancer types^{78,79} such as lung cancer, breast cancer, leukemia/lymphoma, and colorectal cancer. Pain, as it is experienced from cancer patients and especially untreated or inadequately treated pain, can severely impact their physical and psychological health^{80,81}, functional status, and quality of life⁸² of cancer patients. In addition, experienced pain has a negative impact on patients' daily activity, mobility, functioning, sleep quality, entertainment, social interaction, and professional life.^{83,84}

Cancer and ageing

Decision-making for older patients with cancer are a key challenge that can be influenced by many factors, such as the type of cancer, the clinical setting, and patients' fitness and comorbidities. However, treatment decisions should also be based on the patient's baseline quality of life and the estimated risk of impacting it with treatment. In older patients with cancer, it is crucial that for older cancer patients, to consider not only tumour-related factors, but also patient characteristics including functional status, comorbidities, polypharmacy, functional status, mobility, nutritional status, mental health, cognitive status, social support and quality of life, in the context of their preferences.⁸⁵

Finally, cancer early detection for certain cancer types such as breast, colorectal or prostate in the older age group should be considered based on the existing guidelines and individual characteristics of the patient.

Cancer and infectious diseases

Chronic infections with hepatitis B and C viruses have been established as definite causes of hepatocellular carcinoma in humans.⁸⁶ All together, HBV and HCV are responsible for up to 76% of liver cancer cases worldwide,⁸⁷ followed by alcohol consumption, cigarette smoking, diabetes, overweight and aflatoxin B1.⁸⁸ Unlike other forms of cancer, carcinomas caused by viral infections are largely preventable through vaccination or treatments against the chronic infection which precedes and creates the conditions for cancer.⁸⁹ It is important, for example, that the vaccination of infants against hepatitis B be extended to adult risk groups. Furthermore, the awareness for both hepatitis B and C as preventable risk factors, their diagnosis and linkage to care and cure needs to be expanded and strengthened in order to significantly reduce liver cancer's incidence and mortality.⁸⁹

Cancer and alcohol use

The cancer risk associated with alcohol is poorly understood by the public. The harms that result from chronic daily drinking are: the spectrum of alcohol dependency, hypertension, cancer of the gastrointestinal tract, breast, pancreas and liver, preventable nutritional dementia of Wernicke/Korsakoff Syndrome, and teratogenicity to the foetus. All these harms are dose related at an individual level, and alcohol related harm is also dose related at a population level.⁹⁰

Cancer and tobacco use

Tobacco use has a substantial impact on cancer as it accounts for at least 30% of all cancer deaths and 80% of lung cancer deaths.⁹¹ However, smoking heightens the risk of more than 10 types of cancers, including head and neck cancers, leukemia, and cancers of the esophagus, bladder, pancreas, kidney, liver, stomach, colorectum, cervix, uterus, and ovaries.⁹² In fact, tobacco use not only increases the risk of developing various cancers, but also worsens cancer outcomes,⁹³ the survival rates while decreases the therapeutic responses, increases cancer recurrences, and cancer treatment complications, including problems with wound healing, infections, cardiovascular complications, and the development of a secondary malignancy.⁹⁴

Recommendations

Cancer is set to become a top health priority for the next five years in the EU and will play a central role in the policy agenda through the EU Beating Cancer Plan. It is crucial that, with this renewed focus on cancer, we take a comprehensive and integrated care approach to ensure better health outcomes and quality of life for all European patients, independent of age, gender, and state of treatment.



With this work, we call on EU policymakers to prioritise cancer-related complications and comorbidities by:

1. Making cancer-related complications and comorbidities a central part of all policy discussions about cancer care.
2. Including cancer-related complications and comorbidities as an important pillar of the Europe's Beating Cancer Plan implementation which will focus on:
 - 1) Multidisciplinary team working and by taking action to improve HCP training and integrated care by applying already-known methods of addressing cancer-related complications and comorbidities through **an inter-specialty cancer training programme on the management of Cancer-related Complications and Comorbidities.**
 - 2) A new **Knowledge Centre on Cancer** which we expect to put a special attention in research of cancer-related complications and comorbidities during the cancer treatment and survivorship.
 - 3) Including cancer related complications and comorbidities to the '**Better Life for Cancer Patients Initiative**' and to the '**Cancer Survivor Smart-Card**'
 - 4) The creation of a **new European Reference Networks addressing cancer complications and co-morbidities** will be an important step to benefit from cross-border cooperation and EU expertise.
 - 5) Improving **health literacy on cancer risks and determinants** by achieving a tobacco-free Europe, reducing harmful alcohol consumption, improving health promotion through access to healthy diets and physical activity, addressing obesity, reducing

environmental pollution and exposure to hazardous substances and radiation and preventing cancers caused by infections but also look throughout the cancer care journey.

- 6) **Medicines reconciliation**, which has been recognised as a major intervention tackling the burden of medication discrepancies, correcting medication errors and subsequent patient harm at hospital admission and discharge. It allows also identify drug interactions including self-medication with Complementary and Alternative Medicine (CAM). This is particularly acute among cancer patients with comorbidities and complications.
3. Leveraging existing EU funding programs for research on cancer to include cancer-related complications and comorbidities.
4. Proactively coordinating prevention and early detection strategies and establishing fluid communication channels with policymakers, healthcare professionals across several related scientific disciplines, patients and informal carers.
5. Participating in multi-stakeholder dialogue to agree on concrete next steps to address cancer-related complications and comorbidities.
6. Providing policy solutions able to ensure timely access to innovative therapies for all patients as they may have a better impact on health-related outcomes and quality of life.



Eurocarers



European Association for the Study of Obesity (EASO)



European Association of Urology (EAU)



European Brain Council (EBC)



European Cancer Patient Coalition (ECPC) - (Chair)



European Cancer Organisation



European Federation of Neurological Associations (EFNA)



European Federation of Nurses Associations (EFN)



European Geriatric Medicine Society (EuGMS)



European Pain Federation (EFIC)



European Society of Cardiology (ESC)



European Specialist Nurses Organisation (ESNO)



European Thrombosis and Haemostasis Alliance (ETHA)



International Society of Geriatric Oncology (SIOG)



International Society on Thrombosis and Hemostasis (ISTH)



KU Leuven – Leuven Cancer Institute (LKI)



The European Federation of the Associations of Dietitians (EFAD)



The European Nutrition for Health Alliance (ENHA)



The European Society for Clinical Nutrition and Metabolism



The European Society of Surgical Oncology (ESSO)



Obesity Policy Engagement Network (OPEN-EU)



Thrombosis Ireland



Thrombosis UK



International Psycho-Oncology Society



Associations collaborating on hepatitis to immunize and eliminate viruses in Europe



European Association for the Study of the Liver



European Hematology Association



European Society of Oncology Pharmacy



European Network for Smoking and Tobacco Prevention

With the support of unrestricted grants from:



LEO Pharma



Medical Nutrition International Industry



Sanofi



Ipsen – Innovation for patient care



AbbVie



Bristol-Myers Squibb



Pfizer

Endnotes

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