

Making cancer-related complications and comorbidities an EU health priority

Joint statement

Cancer-related complications and comorbidities are a highly significant, and in many cases fatal, burden on patients across Europe but are all too often neglected in policy and research.¹

Cancer is set to become a top health priority for the next five years in the EU, with both the European Commission President, Ursula von der Leyen, and Commissioner for Health and Food Safety, Stella Kyriakides, having made clear that cancer will play a central role in their policy agenda and that the output will be an EU Beating Cancer Plan.

It is time to increase the attention given to cancer patients' long-term well-being and quality of life, addressing the often debilitating comorbidities and complications of cancer, both in terms of the disease itself and its treatments. An increasing population of survivors with needs for long-term follow-up care and management of comorbid conditions will place a substantial burden on health systems, as well as on informal carers who provide essential support to them.

It is crucial that, with this renewed focus on cancer, we take an integrated approach to ensure better health for all European patients.

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

- **Making cancer-related complications and comorbidities a central part of all policy discussions about cancer care.** If adequately addressed, this could significantly improve the quality of life of those living with the diseases and conditions affected, and the well-being of their informal carers, as well as improving treatment outcomes and survivorship. With increased survivorship, comorbidities and complications will soon place an ever-larger burden on healthcare and social welfare systems, and therefore need to be addressed all the more urgently.
- **Including tackling cancer-related complications and comorbidities as an individual pillar in the EU Cancer Plan.** This pillar should focus on:
 - Multidisciplinary team working and by taking action to improve integrated care by applying already-known methods of addressing cancer-related complications and comorbidities.
 - Improving data collection and treatment optimisation, mainly based on post-authorisation research and review of medicines and the use of real-world evidence. Data collection and treatment optimisation should also focus on harmonising and prioritising the tracking of cancer complications and comorbidities in patient information databases on the national level, as a

¹ We define a comorbidity as the co-existence of disorders in addition to a primary disease of interest, and a cancer complication as a complication resulting from the underlying malignancy or its treatment.

Feinstein A. The pre-therapeutic classification of co-morbidity in chronic disease. *J Chronic Dis.* 1970;23:455-469.

Torres V. B. L. et al. Outcomes in Critically Ill Patients with Cancer-Related Complications. *PLoS One.* 2016; 11(10): e0164537.

prerequisite for more deeply integrated collection and sharing of cancer data across the EU. As a first step, it is necessary to count the incidences on cancer complications - something that is not currently done evenly across the EU and can lead to patients seeking treatment in other countries.

- Medicines reconciliation, as there is currently only a relatively limited understanding of the impact that different medicines can have on each other, and this is particularly acute among cancer patients with comorbidities and complications.
- A clear link must also be drawn between the cancer plan EU funding programmes related to cancer, particularly the EU mission on cancer (see next point).
- **Leveraging existing EU funding programs for research on cancer to include cancer-related complications and comorbidities.** The aim is to fill existing gaps in research and establish a more holistic understanding of the impact of these conditions. The EU mission on cancer can be the needed infrastructure for such an action in the framework of the EU's Horizon Europe research programme, running from 2021-2027.
- **Proactively coordinating prevention strategies and establishing fluid communication channels with policymakers, healthcare professionals across several related scientific disciplines and patients.** This will should be done in order to raise awareness among professionals about the need for integrated care and share best practices among Member States. This coordination must also span horizontal integration between technologies and scientific disciplines in order to avoid fragmentation between different cancer types.
- **Participating in multi-stakeholder dialogue to agree concrete next steps to address cancer-related complications and comorbidities.** This open dialogue should include representatives from this initiative, as well as the Commission, Member States, European Parliament, academia, healthcare professionals, industry, patient advocates and other relevant experts. Its findings should then be taken forward by the relevant institutions.

Policy context

- There is currently strong momentum in the EU policy landscape to bring attention to the area of cancer-related complications and comorbidities.
- In particular, the incoming Commission President, Ursula von der Leyen, has pledged to establish the new European Cancer Plan. This could set the agenda of the new Commission and the Parliament. In President von der Leyen’s mission letter to the new Health Commissioner Stella Kyriakides, it is noted that the Cancer Plan “should propose actions to strengthen our approach at every key stage of the disease: prevention, diagnosis, treatment, life as a cancer survivor and palliative care. There should be a close link with the research mission on cancer in the future Horizon Europe programme.”²
- A Cancer Mission is part of Horizon Europe, the EU’s €100 billion research and innovation programme for 2021-2027. The Cancer Mission aims to “defeat cancer”, and “should focus on cancer prevention, cure and quality of life of survivors and ensure that real gains occur in reducing social and regional disparities”.³
- One of the main EU initiatives on cancer during the last mandate was CanCon, which was launched in 2014 by representatives from 17 EU Member States and the Commission’s DG SANTE. CanCon published the European Guide on Quality Improvement in Comprehensive Cancer Control in 2017.⁴ The Guide made several recommendations directly linked to cancer-related complications and comorbidities. It called for setting up Multidisciplinary Comprehensive Cancer Care Networks (CCCNs) to ensure that the management of patients with comorbidities is shared with relevant stakeholders; putting in place a defined pathway on integrated cancer control; and setting up a data collection system to look into the impact and management of comorbidities.
- The actions from CanCon are now addressed by the Innovative Partnership for Action Against Cancer (iPAAC) Joint Action, under the leadership of the German Ministry of Health and the German Cancer Society.⁵ iPAAC was launched in 2018 and aimed to build upon the outcomes of previous Joint Actions. A Roadmap on Implementation and Sustainability of Cancer Control Actions will be the main deliverable of this Joint Action and is expected in April 2020.⁶
- The Commission is also supporting a Joint Action on the implementation of digitally enabled integrated person-centred care, which will be led by Member States.⁷

² Mission letter to Stella Kyriakides, Commissioner-designate for Health. 10 September 2019. https://ec.europa.eu/commission/sites/beta-political/files/mission-letter-stella-kyriakides_en.pdf

³ European Commission. “Commission announces top experts to shape Horizon Europe missions.” 30 July 2019.

https://ec.europa.eu/info/news/commission-announces-top-experts-shape-horizon-europe-missions-2019-jul-30_en

⁴ Albrecht, T., Kiasuwa, R., & Van den Bulcke, M. (2017). European Guide on Quality Improvement in Comprehensive Cancer Control.

⁵ iPAAC (2018)

⁶ Health Programme DataBase - European Commission (2019)

⁷ More info here: https://ec.europa.eu/chafea/health/funding/joint-actions/documents/ja-2019-presentation-02_en.pdf

The burden of cancer-related complications and comorbidities

- Cancer-related complications and comorbidities have a highly significant burden on patients across Europe - in many cases fatal.^{8,9} There is a need to alleviate the burden of cancer-related comorbidities and complications through better risk assessment and treatment, based on a conventional detection approach, which can reduce the number of premature deaths from complications and comorbidities.
 - Comorbidities
 - There are high prevalence rates of comorbid conditions among cancer patients. Research shows that the majority of cancer patients, even up to almost 90% depending on the cancer type and age, report at least one comorbid condition.^{10,11} In addition, cancer patients report more comorbid medical conditions than patients without a history of cancer.¹²
 - Cancer and its treatments have an impact on comorbid conditions. Patients with comorbidities may also suffer higher levels of toxicity from cancer treatments, which can have a detrimental impact on their chances of cancer survival. The relationship also works in the other direction, as both cancer and its treatment can affect comorbidity outcomes. For example, cancer therapies can increase the risk of cardiovascular, metabolic, musculoskeletal, neurological and other conditions, and can worsen pre-existing comorbidities.¹³
 - Patients with comorbidities are less likely to receive treatment with curative intent. This is because there is limited consensus on how to record, interpret or manage comorbidity in the context of cancer. Patients who have comorbidities are less likely to receive treatment with curative intent. Evidence in this area lacks because of the frequent exclusion of patients with comorbidity from randomised controlled trials.¹⁴
 - Patients with comorbidities have a lower life expectancy and experience a poorer quality of life. Several studies have shown that patients with comorbidities have higher mortality than patients without comorbidities¹⁵. Furthermore, comorbidities are negatively associated with multiple indicators of quality of life, including physical functioning, general health, bodily pain¹⁶.

⁸Søgaard, M., Thomsen, R. W., Bossen, K. S., Sørensen, H. T., & Nørgaard, M. (2013). The impact of comorbidity on cancer survival: a review. *Clinical epidemiology*, 5 (Suppl. 1), 3–29. doi:10.2147/CLEP.S47150

⁹Zamorano J.L. et al (2016). 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). *European Journal of Heart Failure*. 19: 9-42. doi: 10.1002/ejhf.654

¹⁰Koroukian SM, Murray P, Madigan E. (2006) Comorbidity, disability, and geriatric syndromes in elderly cancer patients receiving home health care. *J Clin Oncol*.24(15):2304-10. doi: 10.1200/JCO.2005.03.1567

¹¹Lee L., Cheung W.Y, Atkinson E., & Krzyzanowska M.K. (2011). Impact of Comorbidity on Chemotherapy Use and Outcomes in Solid Tumours: A Systematic Review. *Journal of Clinical Oncology*. 29:1, 106-117. doi: 10.1200/JCO.2010.31.3049

¹² Bellizzi K.M. and Rowland J.H. (2007). The Role of Comorbidity, Symptoms and Age in the Health of Older Survivors Following Treatment for Cancer. *Future Medicine. Aging and Health* 3(5):625-635. doi: 10.2217/1745509X.3.5.625

¹³ Sarfati D., Koczwara B. & Jackson C. (2016). The Impact of Comorbidity on Cancer and Its Treatments. *A Cancer Journal for Clinicians*. 2016; 66:337-350. doi: 10.3322/caac.21342

¹⁴Sarfati D., Koczwara B. & Jackson C. (2016). The Impact of Comorbidity on Cancer and Its Treatments. *A Cancer Journal for Clinicians*. 2016; 66:337-350. doi: 10.3322/caac.21342

¹⁵ Piccirillo JF, Feinstein AR. Clinical symptoms and comorbidity: significance for the prognostic classification of cancer. *Cancer*. 1996;77(5):834-842. doi: 10.1002/(SICI)1097-0142(19960301)77:5<834::AID-CNCR5>3.0.CO;2-E.

¹⁶ Malik, Monica & Vaghmare, Rama & Joseph, Deepa & Fayaz Ahmed, Syed & Jonnadula, Jyothi & Valiyaveetil, Deepthi (2016). Impact of Comorbidities on Quality of Life in Breast Cancer Patients. *Indian Journal of Cardiovascular Disease in Women WINCARS*. doi: 10.1055/s-0038-1656491.

- There is a need to build robust healthcare structures to coordinate preventive measures, as well as monitoring strategies throughout the cancer process. Furthermore, healthcare professionals should also be involved in the design of cancer trials to learn how to prevent cardiotoxicity in new targeted therapies.
 - Complications
 - Cancer patients are at risk of severe complications due to the underlying malignancy or its treatment. Cancer and its treatment can cause several complications, including pain, fatigue, pulmonary and cardiovascular diseases, nausea, brain and nervous system problems or unusual immune system reactions. All of these can affect treatment options and their outcomes.
 - Patients with complications have higher mortality rates. They are also more likely to require admission to an intensive care unit (ICU).¹⁷
- There is a lack of screening and integrated care approach. There is low awareness of cancer-related complications and comorbidities among patients, informal carers, ¹⁸ healthcare professionals and policymakers.
- Informal carers provide a substantial portion of care across Europe. While people with cancer are identified through diagnosis, cancer carers often remain largely invisible despite the fundamental role they play in our healthcare systems. They need to be recognised, supported, and fully informed and trained if they wish so.^{19, 20}
- There is not enough data to give an overall picture. Currently there are only data from individual disease areas and conditions (see examples below). This limits the understanding of the true scale of the problem.

¹⁷Torres V.B., Vassalo J, Silva U.V., Caruso P., Torelly A.P., Silva E., Teles J.M., Knibel M., Rezende E., Netto J.J., Piras C., Azevedo L.C., Bozza F.A., Spector N., Salluh J.I. & Soares M. (2016) Outcomes in Critically Ill Patients with Cancer-Related Complications. *PLoS One*. 11(10): e0164537. doi: 0.1371/journal.pone.0164537

¹⁸* Eurocarers defines a carer as a person who provides - usually - unpaid care to someone with a chronic illness, disability or other long-lasting health or care need, outside a professional or formal framework.

¹⁹Eurocarers Cancer Carer toolkit. <https://www.eurocarers-cancer-toolkit.eu/introduction/>

²⁰ ECPC and Eurocarers White Paper on Cancer Carers <http://www.ecpc.org/WhitePaperOnCancerCarers.pdf>

Examples

- **Cancer associated thrombosis (CAT)/ venous thromboembolism (VTE):** Cancer-associated thrombosis (CAT) remains the number one cause of death during chemotherapy and the second-leading cause of all cancer deaths (after disease progression). Cancer patients are estimated to have a 2- to 20-fold higher risk of developing venous thromboembolism (VTE) than non-cancer patients²¹. VTE is a leading cause of death and disability worldwide.²² Up to 60 percent of VTE cases occur during or after hospitalisation, making it a leading preventable cause of hospital death.²³ In Europe, there are 544,000 VTE-related deaths every year.²⁴ It is a life-changing and traumatic event, even without the complication of having cancer. Therefore, the devastation that it can cause to survivors should not be under-estimated, particularly among those that have already been given a life altering cancer diagnosis. There needs to be investment in VTE information, recovery & support programs for patients.
- **Cardiovascular system:** Most risk factors for cancer and cardiovascular diseases are the same. Due to ageing a large part of population has coexisting cancer and cardiovascular diseases. An active cancer strongly complicates the management of many cardiovascular diseases and lead to heavy ethic decisions (e.g.: high invasive and costly therapy in cancer patients with uncertain prognosis). Most cancer treatments may lead to a cardiovascular complication (heart failure, coronary artery diseases, arrhythmias, stroke, etc.) which may occur acutely during treatment administration or also after many years requiring a tight long-term follow-up. Cardio-oncology is a relatively new subspecialty facing prevention, identification and management of these toxic effects.
- **Mental health:** Depression is a comorbid disabling syndrome that affects approximately 15% to 25% of cancer patients²⁵. Only 20% of people with cancer who also have anxiety and/or depression are recognised as having a mental health disorder and receive appropriate treatment²⁶. Besides, some cancer patients (particularly those with head and neck cancer, which have the highest incidence of suicide in all oncology populations) are at high risk for developing depressive symptoms and a major depressive disorder as comorbidities²⁷.
- **Neurologic complications:** Cancer often affects the nervous system and may result in significant neurologic morbidity and mortality. These effects may be direct—with direct cancer involvement of the brain, spine, or peripheral nervous system (PNS)—or indirect as in paraneoplastic neurologic syndromes. Around 15-20% of cancer patients have neurological complications during their illness²⁸. Treatment of cancer can also damage the nervous system²⁹; Chemotherapy-induced peripheral neuropathy (CIPN) is a common dose-limiting side effect experienced by patients receiving treatment for cancer.³⁰ Complications are associated with age; the impact will depend on several issues such as tolerance of treatment, development of persisting or late toxicity, and the influence of other

²¹ECPC & LEO Pharma. Cancer- Associated Thrombosis (CAT), A neglected cause of cancer death: actions needed to increase health outcomes and reduce mortality.

²² <https://www.worldthrombosisday.org/issue/vte/>

²³ Jha AK, Larizgoitia I, Audera-Lopez C, Prasopa-Plaisier N, Waters H, Bates DW. The global burden of unsafe medical care: analytic modeling of observational studies. *BMJ Qual Saf* 2013; 22:809-15. Retrieved from: <http://qualitysafety.bmj.com/content/22/10/809.full.pdf+html>

²⁴ Heit, JA. Poster 68 presented at: American Society of Hematology, 47th Annual Meeting, Atlanta, GA, December 10-13, 2005.

²⁵[US] National Cancer Institute. Depression (PDQ®)-Health Professional Version.

²⁶Cohen, A. (WHO) (2017) Addressing comorbidity between mental disorders and major noncommunicable diseases.

²⁷Friedland C.J. (2019) Head and Neck Cancer: Identifying Depression as a Comorbidity Among Patients. *Clinical Journal of Oncology Nursing*

²⁸Barrow Neurological Institute (2017). Neurologic Complications of Cancer.

²⁹Giglio, P., & Gilbert, M. R. (2010). Neurologic complications of cancer and its treatment. *Current oncology reports*, 12(1), 50-59. doi: 10.1007/s11912-009-0071-x

³⁰ Nathan P. Staff, MD, PhD, Anna Grisold, MD, Wolfgang Grisold, MD, and Anthony J. Windebank, MD (2017). Chemotherapy-Induced Peripheral Neuropathy: A Current Review

concomitant diseases.³¹ With improved cancer treatments and longer survival, the late effects of CIPN continue to affect cancer survivors.³²

- **Obesity:** There is consistent evidence that people living with obesity have an increased risk of developing several types of cancer.³³ This can have a significant impact on patients, impacting the cancer progression, quality of life, survivorship and likelihood of recurrence.^{34, 35} This is particularly important in Europe, as the percentage of new cancer cases attributable to overweight and obesity is higher in the region than the global average.³⁶

³¹ Grisold W., Grisold A. Loscher W.N. (2016) Neuromuscular complications in cancer. doi: <https://doi.org/10.1016/j.jns.2016.06.002>

³² Nathan P. Staff, MD, PhD, Anna Grisold, MD, Wolfgang Grisold, MD, and Anthony J. Windebank, MD (2017). Chemotherapy-Induced Peripheral Neuropathy: A Current Review

³³ Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body Fatness and Cancer--Viewpoint of the IARC Working Group. *New England Journal of Medicine* 2016; 375(8):794-798. doi: 10.1056/NEJMs1606602

³⁴ Calle EE, Rodriguez C, Walker-Thurmond K, Thun M. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *New England Journal of Medicine* 2003; 348(17):1625-1638.

³⁵ Schmitz KH, Neuhauser ML, Agurs-Collins T, et al. Impact of obesity on cancer survivorship and the potential relevance of race and ethnicity. *Journal of the National Cancer Institute* 2013; 105(18):1344-1354.

³⁶ WHO Regional Office for Europe, "High cancer burden due to overweight and obesity in most European countries" (2014). <http://www.euro.who.int/en/health-topics/health-determinants/gender/news/news/2014/11/high-cancer-burden-due-to-overweight-and-obesity-in-most-european-countries>



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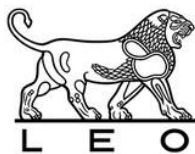
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