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, including gateaway diseases which can lead to cancer, as well as 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 complications and 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 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 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 prevent cancer, 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 but also measuring

[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.

processes of care by well-defined indicators (i.e. guideline compliance). Data collection and treatment optimisation should also focus on harmonising and prioritising the tackling of acute infections which can lead to cancer, tracking of cancer complications and comorbidities in patient information databases on the national level, as a prerequisite for more deeply integrated collection and sharing of cancer data across the EU. As a first step, it is necessary to measure the incidence of cancer related morbidity – 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 as well as medication-nutrition interactions, and this is particularly acute among cancer patients with comorbidities and complications.

- Equitable access to nutrition and nutritional care as an integral part of comprehensive care for all cancer patients with a focus on ageing patients, is a key condition to reduce complications and comorbidity, maintaining optimal health and quality of life[2] [3].

- Patient involvement in every aspect of the comprehensive care is essential, applying aspects of shared decision making[4] not least for nutritional care.

- 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 should be done in order to raise awareness among professionals about the need to tackle infections and/or gateway diseases through improved diagnosis, linkage to care and monitoring, 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.

[2] EPF position statement on information to patients on food and nutrition. https://www.eu-patient.eu/globalassets/policy/nutrition/epf-position-statement---nutrition.pdf
[3] Ljungqvist O, de Man F. Undernutrition: a major health problem in Europe. Nutr Hosp 2009;24:369-70.
[4] Van de Pol, M, et al. Expert and patient consensus on a dynamic model for shared decision making in frail older patients, Journal for Patient Education and Counseling, 2016

Policy context

- There is currently a strong momentum in the EU policy landscape to bring attention to the area of cancer-related complications and comorbidities.

- In particular, the 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."[5]

- 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".[6]

- 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.[7] 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.[8] 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.[9]

- 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.[10]

[5] 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
[6] 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
[7] Albreht, T., Kiasuwa, R., & Van den Bulcke, M. (2017). European Guide on Quality Improvement in Comprehensive Cancer Control.
[8] iPAAC (2018)
[9] Health Programme DataBase - European Commission (2019)
[10] 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 add a highly significant burden on patients across Europe – and are in many cases fatal.[11, 12] 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 suffering and 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.[13, 14] in addition, cancer patients report more comorbid medical conditions than patients without a history of cancer.[15]
        - 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 survival following cancer treatment. 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.[16]
        - Equitable access to healthy food and nutritional care paired with early, meaningful patient involvement will significantly drive effective disease management. There is strong evidence that loss of muscle mass increases the risk of peri-operative complications, early cessation of chemotherapy and mortality and decreases quality of life.[17]. Good nutritional status and optimal nutritional care including dietary counseling contribute to better health outcomes, clinical outcomes and quality of life.
        - 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. Evidence in this area is lacking because of the frequent exclusion of patients with comorbidity from randomised controlled trials.[18]

[11]Søgaard, 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

[12]Zamorano 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

[13]Koroukian 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

[14]Lee 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

[15] 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

[16] 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

[17]Arends J , Bachmann P , Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017 Feb;36(1):11-48.

[18]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

- 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 comorbidities[19]. Furthermore, comorbidities are negatively associated with multiple indicators of quality of life, including nutritional status, physical functioning, general health and pain[20].

- There is a need to build robust social- and healthcare structures to coordinate preventive measures, as well as monitoring strategies throughout the cancer process. Furthermore, healthcare professionals and patients should also be involved in the design of cancer trials to learn how to prevent or reduce toxicities such as cardio and gastrointestinal toxicity in new targeted therapies.

- Patients and their carers need to be better informed about treatment, support and self management options[21].

  - 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, gastrointestinal, pulmonary and cardiovascular diseases, nausea, brain and nervous system problems or unusual immune system reactions and malnutrition (i.e. undernutrition). All of these can affect treatment options and their outcomes.

    - Patients with complications have higher mortality rates. They are also more likely to require admissions to hospitals and to intensive care units (ICUs).[22]

- There is a lack of screening and integrated care approach. Screening and assessment of nutritional status is vital to initiate treatment that reduces the number of malnutrition-related complications and poor outcomes. Also screening of malfunctioning of other organs is important for among other autoimmune disease. There is low awareness of cancer-related complications and comorbidities among patients, informal carers,[23] 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 appropriately informed and trained if they wish so.[24, 25]

[19] 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.

[20] Malik, Monica & Vaghmare, Rama & Joseph, Deepa & Fayaz Ahmed, Syed & Jonnadula, Jyothi & Valiyaveettil, 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.

[21] European Patients' Forum, https://european-nutrition.org/good-practices/how-to-involve-patients-in-guidelines/

[22] Torres 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

[23] * 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.

[24] Eurocarers Cancer Carer toolkit. https://www.eurocarers-cancer-toolkit.eu/introduction/

[25] ECPC and Eurocarers White Paper on Cancer Carers http://www.ecpc.org/WhitePaperOnCancerCarers.pdf

- 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.

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 patients[26]. VTE is a leading cause of death and disability worldwide.[27] Up to 60 percent of VTE cases occur during or after hospitalisation, making it a leading preventable cause of hospital death.[28] In Europe, there are 544,000 VTE-related deaths every year.[29] 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 patients[30]. Only 20% of people with cancer who also have anxiety and/or depression are recognised as having a mental health disorder and receive appropriate treatment[31]. 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 comorbidities[32].

- **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 illness[33].Treatment of cancer can also damage the nervous system[34]; Chemotherapy-induced peripheral neuropathy (CIPN) is a common dose-limiting side effect experienced by patients receiving treatment

[26]ECPC & LEO Pharma. Cancer- Associated Thrombosis (CAT), A neglected cause of cancer death: actions needed to increase health outcomes and reduce mortality.
[27] https://www.worldthrombosisday.org/issue/vte/
28 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
[29] Heit, JA. Poster 68 presented at: American Society of Hematology, 47th Annual Meeting, Atlanta, GA, December 10-13, 2005.
[30][US] National Cancer Institute. Depression (PDQ®)–Health Professional Version.
[31]Cohen, A. (WHO) (2017) Addressing comorbidity between mental disorders and major noncommunicable diseases.
[32]Friedland C.J. (2019) Head and Neck Cancer: Identifying Depression as a Comorbidity Among Patients. Clinical Journal of Oncology Nursing
[33]Barrow Neurological Institute (2017). Neurologic Complications of Cancer.
[34]Giglio, 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

for cancer.[35] 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 concomitant diseases.[36] With improved cancer treatments and longer survival, the late effects of CIPN continue to affect cancer survivors.

- **Malnutrition (undernutrition):** Many cancer patients have a normal weight or are even overweight or obese, but still have a significant weight loss and underlying hidden sarcopenia (i.e. characteristics of malnutrition) which is responsible for the poor outcomes related to malnutrition[16]. It is estimated that the deaths of 10-20% of patients with cancer can be attributed to malnutrition rather than to the malignancy itself. Thus, nutrition is an important aspect of multimodal cancer care. Yet, recent studies in European hospitals found that only 30%-60% of patients with cancer who were at risk of malnutrition actually received nutritional support (i.e., oral nutritional supplements, enteral and/or parenteral nutrition).[37]

- **Obesity:** There is consistent evidence that people living with obesity have an increased risk of developing several types of cancer.[38] It is not only having more fat mass that causes comorbidities or complications but the lack of muscle mass while being overweight i.e. sarcopenic obesity, This can have a significant impact on patients, impacting the cancer progression, quality of life, survivorship and likelihood of recurrence.[39, 40] 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.[41]

- **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 chronic widespread pain induced by plastic changes in the sensory nervous system.[42] Improved early cancer diagnosis and enhanced treatments will continue to enable many patients to live with cancer as a chronic disease. In patients who survive cancer or in those who live with progressive advanced disease, pain is a very common symptom and affects up to 40% of cancer survivors and at least 66% of patients with advanced progressive disease. Between 33% and 40% of cancer survivors suffer from chronic pain and studies have shown that at least one-third of patients are often undertreated due to inadequate attention to pain during regular oncological treatment, and unfair or delayed access to opioids.[43,44,45,46] Some of these patients will continue to experience pain that negatively affects their

[35] Nathan P. Staff, MD, PhD, Anna Grisold, MD, Wolfgang Grisold, MD, and Anthony J. Windebank, MD (2017). Chemotherapy-Induced Peripheral Neuropathy: A Current Review
[36] Grisold W., Grisold A. Loscher W.N. (2016) Neuromuscular complications in cancer. doi: https://doi.org/10.1016/j.jns.2016.06.002
[37] Arends J, Baracos V, Bertz, H, et al. ESPEN expert group recommendations for action against cancer related malnutrition. Clinical Nutrition 2017; 36:1187-1196.
[38] 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/NEJMsr1606602
[39] Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. 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.
[40] Schmitz KH, Neuhouser 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.
[41] 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
[42] Kosek, E., Cohen, M., Baron, R., Gebhart, G. F., Mico, J.-A., Rice, A. S.C., Rief, W., Sluka, A. K. (2016). Do we need a third mechanistic descriptor for chronic pain states? Pain, 157(7), 1382–1386. https://doi.org/10.1097/j.pain.0000000000000507
[43] Greco MT, Roberto A, Corli O, Deandrea S, Bandieri E, Cavuto S, Apolone G. Quality of cancer pain management: an update of a systematic review of undertreatment of patients with cancer. J Clin Oncol. 2014;32(36):4149–54. https://doi.org/10.1200/jco.2014.56.0383.
[44] Te Boveldt ND, Vernooij-Dassen MJ, Jansen A, Vissers KC, Engels Y. Pain is not systematically registered in Dutch medical oncology outpatients. Pain Practice 2015; 15(4):364–370.
[45] Gagnon B, Scott S, Nadeau L, Lawlor PG. Patterns of community-based opioid prescriptions in people dying of cancer. J Pain Symptom Manage 2015; 49(1): 36–44.
[46] Ziegler L, Mulvey M, Blenkinsopp A, Petty D, Bennett MI. Opioid prescribing for patients with cancer in the last year of life: a longitudinal population cohort study. Pain 2016; 157(11):2445–51.

quality of life and some patients may continue to use high doses of opioids, previously required for adequate pain control, which are no longer needed while causing severe side effects.[47]

- **Coelic disease:** Lymphomas, mostly T-cell type, and other malignant tumours, particularly carcinoma of the small bowel, less frequently of stomach and oesophagus, are associated with coeliac disease (CeD).[48] If diagnosed only in adults or with substantial delay, the risk for complications increases. Depending on the diagnostic latency or non-adherence to the therapy, some of these long-term consequences are only partly reversible. If untreated they still may develop long-term health consequences later in life. If symptoms and signs of CeD do not resolve or re-occur on a gluten-free diet, there is also a severe but rare complication called refractory celiac disease (RCD), also called refractory sprue.[49]

- **Viral hepatitis and cancer:** Viral Hepatitis B and C are responsible for up to 76% of liver cancer cases worldwide.[50] In the European Union, around 10 million people live with chronic Hepatitis and a majority are undiagnosed.[51] Every year up to 90,000 of them develop liver cancer,[52] which has the lowest survival rate among all cancers monitored by the European Commission,[53] making it the deadliest preventable cancer in the EU. Cancer prevention efforts targeting viral Hepatitis could reduce liver cancer incidence by 70% and liver-related death by 65%,[54] especially among high-risk groups who are associated with higher incidence rates.[55] The Hepatitis B infant vaccination programmes must thus be complemented by vaccination programmes for risk groups. In addition to vaccinations, measures must be put in place to systematically increase the diagnosis of people with viral Hepatitis B and C and to ensure their linkage to treatment and care, and their monitoring along the cascade of care, in order to prevent and reduce the burden of liver cancer and other hepatitis-associated cancers, including kidney, colorectal, pancreatic, gallbladder and biliary duct and ovarian cancer.[56]

- **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.[57] We estimate the increase in absolute risk of cancer secondary to moderate levels of alcohol, and compare these to the risk associated with low levels of smoking, creating a 'cigarette-equivalent of harm. One bottle of wine per week is associated with

[47] Bennett MI, Eisenberg E, Ahmedzai SH, Bhaskar A, O'Brien T, Mercadante S, Škvarč NK, Vissers K, Wirz S, Wells C, Morlion B. Standards for the management of cancer-related pain across Europe. A position paper from the EFIC Task Force on Cancer Pain. European Journal of Pain 2019; 23:660–668.
[48] Malignant complications of coeliac disease, - N.Brousse J.W.R. Meijer)Best Practice & Research Clinical Gastroenterology Volume 19, Issue 3, June 2005, Pages 401-412.
[49] Classification and Management of Refractory Celiac Disease - Alberto Rubio-Tapia, MD and Joseph A Murray MD: Gut. 2010 Apr; 59(4): 547–557.
[50] Wild, C. P. (WHO) (2020). World Cancer Report. Cancer Research for Cancer Prevention, p. 61.
[51] European Parliament, Background note on lifestyle-related and vaccine-preventable risk factors and prevention strategies, 2020; ECDC: around 9 million Europeans are affected by chronic hepatitis B or C. Accessed from https://www.ecdc.europa.eu/en/news-events/ecdc-around-9-million-europeans-are-affected-chronic-hepatitis-b-or-c
[52] International Agency for Research on Cancer (WHO) (2020). Liver Cancer Fact Sheet. Accessed from https://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf
[53] Joint Research Centre (European Commission). European Cancer Information System – ECIS. Estimates of cancer incidence and mortalility in 2020, for all cancer sites. Accessed from https://ecis.jrc.ec.europa.eu/explorer.php?$0-0$1-AE27$2-All$4-1,2$3-All$6-0,85$5-2008,2008$7-7,8$CEstByCancer$X0_8-3$CEstRelativeCanc$X1_8-3$X1_9-AE27$CEstBySexByCancer$X2_8-3$X2_-1-1
[54] European Union HCV Collaborators. (2017). Hepatitis C virus prevalence and level of intervention required to achieve WHO targets for elimination in the European Union by 2030: a modelling study. *Lancet Gastroenterol Hepatol, 2*(5), pp. 325-336.
[55] European Cancer Organisation. (2020) It Can Be Done – Beating Inequalities in Cancer Care. Action Report. Accessed from https://www.europeancancer.org/resources/164:beating-inequalities-in-cancer-care.html
[56] Wei, M. T., Henry, L., Nguyen M. H. (2019). *Nonliver Comorbidities in Patients with Chronic Hepatitis B. Clinical Liver Disease 14*(3), pp. 126-130.
[57] Nick Sheron, Alcohol and liver disease in Europe – Simple measures have thepotential to prevent tens of thousands of premature deaths, Journal of Hepatology 2016 vol. 64 | 957–967

an increased absolute lifetime cancer risk for non-smokers of 1·0% (men) and 1·4% (women). Among 1,000 individuals drinking at this level, we estimate an additional ten cancers for men, 14 for women. The overall cancer risk for one bottle of wine per week equals that of five (men) or ten cigarettes per week (women). Gender differences result from moderate levels of drinking leading to 0·8% absolute risk of breast cancer in female non-smokers Conclusions: One bottle of wine per week leads to an increased absolute lifetime risk of alcohol-related cancers in women, driven by breast cancer, equivalent to the overall cancer risk associated with ten cigarettes per week. These findings can help communicate that moderate levels of drinking are an important public health risk for women. The risks for men, equivalent to five cigarettes per week, are also of note.[58]

- **Tobacco use and cancer:** 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.[59] 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.[60] In fact, tobacco use not only increases the risk of developing various cancers, but also worsens cancer outcomes,[61] 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. [62]

Eurocarers

The European Association for the Study of Obesity (EASO)

The European Association of Urology (EAU)

The European Brain Council (EBC)

The European Cancer Patient Coalition (ECPC) (Chair)

The European Cancer Organisation (E.C.O.)

[58] Hydes, T.J., Burton, R., Inskip, H. et al. A comparison of gender-linked population cancer risks between alcohol and tobacco: how many cigarettes are there in a bottle of wine?. BMC Public Health 19, 316 (2019). https://doi.org/10.1186/s12889-019-6576-9

[59] American Cancer Society 2012. Cancer facts & figures 2012. 2012. http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf .

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The European Federation of Neurological Associations (EFNA)

The European Society of Surgical Oncology

The European Hematology Association (EHA)

The European Federation of Nurses Associations (EFN)

The European Geriatric Medicine Society (EuGMS)

The European Pain Federation (EFIC)

The European Society of Cardiology (ESC)

The European Specialist Nurses Organisation (ESNO)

The European Thrombosis and Haemostasis Alliance (ETHA)

The International Society on Thrombosis and Hemostasis (ISTH)

The 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

Thrombosis Ireland

Thrombosis UK

The International Psycho-Oncology Society (IPOS)

The International Society of Geriatric Oncology (SIOG)

The European Association for the Study of the Liver (EASL)

The European Society of Oncology Pharmacy (ESOP)

The European Network for Smoking and Tobacco Prevention (ENSP)

The Associations collaborating on hepatitis to immunize and eliminate viruses in Europe (ACHIEVE)

The EU Obesity Policy Engagement Network (OPEN-EU)

Global Alliance of Mental Illness Advocacy Networks-Europe (GAMIAN-Europe)

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