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Mostly Cancer

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1. CANCER AND THE OLDEST OLD

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1.1. INTRODUCTION

As we move through the 21st century, the global population make-up is ageing. In other words, there are more over 65s alive and this will continue to rise, along with the "oldest old" (over 80s). "This rise in longevity is accompanied by a projected increase in the incidence of several conditions, including cancer. While cancer risk inherently increases with age, epidemiological studies on cancer in older populations usually group all patients aged 65 and above into a single category, without specifically examining the oldest old and their distinct characteristics" (Jean et al 2026).

Shah et al (2025) reported an analysis specifically of the oldest old; estimating 2.6 million new cancer cases globally (ie: 14% of total global cases), and 2.1 million cancer deaths (22% of all cancer deaths) in 2022. A prediction of 7.4 million and 6 million respectively in this age group by 2050 [1].

Predictions are important for future planning and preparation, especially for poorer countries, as Shah et al (2025) explained: "Although less-resourced countries currently have a younger population compared with higher-income countries, they will experience the largest increases in new cancer diagnoses and deaths in the oldest old following the rapid ageing of their population. This growing burden will further strain healthcare systems with limited resources, including skilled staff, particularly in oncology and geriatrics, as well as infrastructure and access to treatment. Even if it is not specific to the oldest old, the increasing cancer burden worldwide will lead to an increasing need for supportive and palliative care, including pain management, which may raise some issues since many low-income countries have limited access to opioids and palliative care services. It is essential countries proactively plan and prepare to face this growing burden" (p5).

[1] The data came from Globocan (Global Cancer Observatory) of the WHO (https://gco.iarc.fr/en).

Jean et al (2026) introduced a special issue of the journal "Cancer Epidemiology" on cancer in the oldest old with this important observation: "The oldest old are a heterogeneous group in terms of health status and fitness, and age alone cannot guide cancer management or predict cancer outcomes in this population. Furthermore, this population often presents with a higher prevalence of co-morbidities and increased frailty..." (p1). Undertreatment was a key issue. For example, around one-quarter of women with ovarian cancer over 80 received a combination of surgery and chemotherapy compared to three-quarters of women under seventy years old (Barben et al 2025) (table 1.1).

Delays in treatment was another issue for the oldest old cancer diagnoses, while most information about this age group came from studies in richer countries (Jean et al 2026).

- The data came from Cote d'Or in Northeast France for 1998 to 2018. The Cote d'Or breast and gynaecological cancer registry, initiated in 1982, records all cases of breast and gynaecological cancers diagnosed in residents of Cote d'Or by collecting comprehensive population-based data at the time of diagnosis" (Barben et al 2025 p2).

- The total number of epithelial ovarian cancer cases in the region was 721 in the study period, and 24% of them were in their 70s, and 12% aged eighty years and above.

- Comparing all patients in terms of treatment offered, there was a significant reduction in use of surgery and chemotherapy with age. A combination of these treatments was given to 73% of women aged below 70 years, 62% of 70-79 year-olds, and 27% of women aged eighty and above. Some information about the older patients was missing, which might explain the treatment decisions made (Barben et al 2025).

- The five-year net survival (NS) rate was nearly half for younger women (below 70 years), and around 20% for the oldest old. "The oldest patients had less optimal treatment and a lower NS compared to patients in their seventies or younger", concluded Barben et al (2025 p1).

Table 1.1 - Barben et al (2025).

1.2. UNDERTREATMENT AND DELAYS

Nonagenarians are ninety years and above, and their number is increasing, but they are under-represented in the cancer literature, "especially in clinical trials, often because of their co-morbidities. In studies that

enrolled older participants, the sub-groups data are often missing. Thus, scientific data is lacking for this population and, because of the frailty and heterogeneity of this population, the efficiency of some treatment in younger patients may not be generalised to older patients" (Guerin et al 2025 p2).

It is estimated that 25-50% of cancer patients of this age group receive treatment, and surgery and radiotherapy are the dominant forms (Guerin et al 2025).

Guerin et al (2025) reported the data on 119 nonagenarians at a French Comprehensive Care Centre between 2019 and 2023. Despite being able to live independently, the cohort had severe con-morbidities (ie: other diseases than the cancer), and polypharmacy, and malnutrition was common. The specialist oncogeriatric team recommended different treatments depending on the individual (eg: 27% received radiotherapy; 25% supportive care only). The six-month survival probability was 70%, but this varied depending on the treatment. The researchers concluded that "anti-cancer treatments were carried out with few early treatment failures" (Guerin et al 2025 p1). This was a retrospective study.

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma, and age is an unfavourable variable for survival here. "Older adults are also more likely to present poor performance status (PS) at diagnosis, the latter being highly associated with lower survival. Care management in the older population may be challenging due to the presence of co-morbidities, impaired functional and/or cognitive status, and a higher risk of treatment toxicities. In addition, the poor rate of inclusion of older adults in clinical trials does not facilitate treatment decision-making. Thus, poorer outcomes among older patients with DLBCL may result from an interplay of unfavourable biology of the disease, poor health status, sub-optimal management, treatment toxicities, and unmet treatment needs in this population" (Cantrelle et al 2025 p2).

But is there difference between the oldest and youngest old in terms of DLBCL? Cantrelle et al (2025) used French data from the REALYSA study, began in November 2018, to answer this question. This was a retrospective analysis of data for 560 DLBCL patients sub-divided into three groups - 60-69 years, 70-79 years, and 80 years and above. For each patient, age at diagnosis, socio-demographic factors, social support, living-area related factors (eg: deprivation; access to health care services), health-related factors (eg: co-

morbidities), clinical factors (ie: cancer specifics), and geriatric assessment (eg: frailty) were recorded.

In terms of differences between the age groups, co-morbidity increased with age, and "the oldest patients were more likely to have high-risk disease and geriatric frailty at diagnosis" (Cantrelle et al 2025 p1). The oldest old were more likely to be single, have lower education level, live in more deprived areas, and have less physical exercise than the younger groups.

The oldest old were less likely to be receiving treatment at three months after diagnosis than the younger patients. The researchers emphasised the need for more research to explain this delay between diagnosis and treatment.

The sample in the study include only individuals receiving treatment, and only 14% of the total were the oldest old.

Semprini et al (2025) reported an increasing proportion of cancers diagnosed at a later stage in the oldest old in Puerto Rico, and in US States with large Hispanic/Latino populations between 2005 and 2021. The data were taken from the US Cancer Statistics database as the main source, and 85 years and above was the cut-off for oldest old in this study. Puerto Rico was compared to nine US States with large enough data sets of old Hispanic/ Latino individuals.

Overall, annual cancer incidence and mortality rates in Puerto Rico for the oldest old were declining (and for males the decline was greater than in the US States). "While significant progress has been made in reducing cancer incidence and mortality among Puerto Rico's oldest residents, challenges persist. Policies improving healthcare access could help reduce the burden of cancer incidence and mortality among Puerto Rico's ageing population. Data revealing disaggregated ethnicity and nationality beyond Hispanic/Latino could further inform targeted efforts to advance cancer equity across the US" (Semprini et al 2025 p1).

Semprini et al (2025) commented: "Puerto Rico's population is predominantly composed of long-established individuals, resulting in a relatively homogeneous demographic. In contrast, Hispanic/ Latino populations in mainland US are highly diverse, encompassing individuals of Mexican, Cuban, Central American, South American, and other origins. This diversity leads to variations in cultural practices, socio-economic status, and health behaviours, all of which can influence ageing patterns and cancer epidemiology. Research indicates significant

disparities in cancer mortality rates among different Hispanic sub-groups" (p6).

The researchers made this further point about "the accuracy of age reporting. In some populations, particularly among migrants, age misclassification is common due to inaccurate birth records or strategic misrepresentation for immigration purposes. Puerto Rico, in contrast, has a well-established civil registry system, potentially leading to more accurate age reporting. This may partially explain differences in cancer rates between Puerto Rico and Hispanic/Latino populations in mainland states, where fluctuations in migration patterns and return migration at older ages may distort cancer mortality statistics" (Semprini et al 2025 pp6-7).

1.3. GLOBAL ISSUES

Trachea, bronchus, and lung (TBL) cancer is the leading cause of cancer-associated mortality in he world (Chen et al 2025). Chen et al (2025) analysed the "Global Burden of Disease" (GBD) data for 1992 to 2021 for over 60s and TBL cancer. The GBD is collated by the World Health Organisation from data provided by 204 countries and territories, and each country is divided into five quintiles on the socio-demographic index (SDI) (eg: based on income per capita; years of education on average).

The burden of TBL cancer "varies widely across different regions and demographics" (Chen et al 2025 p1). For example, East Asia in 2021 had "a substantial TBL cancer burden" (p1), and Western Sub-Saharan Africa showed a "noted increase" (p1) over the study period, while Monaco and Greenland were high burden individual countries [2] (appendix 1A).

The 85-89 years group was most affected of all over 60s, and poorer regions, and women generally had "a particularly notable increase in burden" (Chen et al 2025 p1). Smoking followed by particulate air pollution were key risk factors in TBL cancer-related deaths.

de Vries et al (2025) analysed WHO data on seven

[2] "The cancer profile in the oldest old varies by sex, region, and income level, reflecting the lifelong exposure to cancer risk factors that are different across settings. For example, Oceania has the highest melanoma rates globally due to high ultraviolet ray exposure, while elevated liver cancer rates in China and parts of Asia are linked to high prevalence of Hepatitis B and C. In India and Africa, higher human papillomavirus (HPV) infection rates and lower HPV vaccination rates contribute to increased cervical cancer incidence. High stomach cancer rates in China and Asia reflect the interplay of genetics, diet, and healthcare access" (Shah et al 2025 p5).

cancer types among the "older segments of the population" (over 70s) in South America since 1985. Overall, cancer mortality rates were declining over time, though there was great variety between the nine countries studied [3]. "Across all cancer types, mortality rates exhibit a sharp increase with age, with individuals aged 85 and above often experiencing rates nearly double those of the 70–74 age group. The difference in mortality between countries with the lowest rates (eg: Paraguay and Argentina for both sexes) versus those with the highest rates (eg: Venezuela, Chile, Brazil, and Uruguay for males; Peru, Chile, Colombia, and Brazil for females) was more than two-fold" (de Vries et al 2025 p3) [4]. Lung cancer was the primary cause of cancer deaths in most of the countries.

The WHO Cancer Mortality Database was the source of the data used, and its content is only as good as the data provided annually by the official statistics department of a country's government.

1.4. APPENDIX 1A - GLOBAL ONCOLOGY

Surawy Stepney et al (2025) made reference to "Global Oncology", which is "generally understood as a set of interventions that aim to 'close the divide' in 'cancer access and outcomes' by addressing 'disparities and differences in cancer prevention, care, research, education and the disease's social and human impact around the world'" (p1). It emerged as a field in the 1990s (Surawy Stepney et al 2025).

But Global Oncology faces three key challenges according to Surawy Stepney et al (2025): "the overwhelming dominance of Global North countries in setting the terms of Global Oncology, its aspirations and curricula; the imposition of standards, tools and procedures that are often out of touch with situations on the ground; and a characterisation of global cancer care which obscures more complex dynamics of difference and inequality" (p1).

Wider issues include the "brain drain" of health

[3] "Changes over time in cancer rates may be due to changes in risk factors and quality of available treatments, but may also be due partially to improvements in access to cancer care, detection, and registration practices. As possibilities of online data-sharing and data checks as well as awareness of the importance of training in coding practices of mortality data have likely improved over time, these improvements may explain some part of the observed trends" (de Vries et al 2025 p16).

[4] "Variations in mortality rates depend on countries' disease profiles and the quality of their mortality statistics. Exposure to risk factors, cancer incidence, access to healthcare, screening programs, and socioeconomic factors contribute to the diversity in mortality rates between countries" (de Vries et al 2025 p5).

workers and expertise from the Global South to the Global North. "However, even when experts return to countries in the South, these actors do not necessarily usher in a change of oncology agendas but may be more inclined to perpetuate existing frameworks and expertise set in the North" (Surawy Stepney et al 2025 p2).

Surawy Stepney et al (2025) favoured "not the spread of a singular, monolithic 'global oncology', but numerous different 'oncologies', embedded in and cognisant of the epistemologies, politics and care infrastructures of individual locations. Whereas recent critics of Global Oncology have argued that the future of the field is one 'beyond borders' [Ayodele 2024] — a universalising phenomenon that unites diverse communities in the common vision of reducing equity gaps — we encourage policymakers and physicians to 'provincialise oncology' [Chakrabarty 2000] — to locate it within a particular place and context, and rob it of its supposed universal or transcendental character as the only oncology" (p2).

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2. CIGARETTE SMOKING CESSATION AFTER CANCER DIAGNOSIS

2.1. Introduction
2.2. Cessation
2.3. Second primary cancer
2.4. Advice from health professionals
2.5. Screening
2.6. Unhealthy behaviours
2.7. Appendix 2A - Vaping
    2.7.1. Packaging
    2.7.2. Swap to Stop
2.8. Appendix 2B - Alcohol consumption
2.9. References

2.1. INTRODUCTION

Introducing the special supplement of the journal "Cancer Epidemiology" on smoking cessation after a cancer diagnosis, Smith et al 2022) summarised a number of key issues, including the effects of smoking cessation after cancer diagnosis, smoking relapse, cessation programmes in hospital (and out), and e-cigarette use. Only one study in the supplement involved a low or middle income country, the authors lamented: "Implementation of tobacco cessation programmes in such settings, often with populations with high smoking prevalence requires special attention" (Smith et al 2022 p2).

2.2. CESSATION

"Continued smoking after a cancer diagnosis impacts treatment efficacy, tolerability to medications, and patient quality of life; and increases the risks of recurrence or development of new primaries" (Hawari et al 2022 p1). Quitting after a cancer diagnosis (irrelevant of the type of cancer) is associated with higher survival rates (Hawari et al 2022) [5].

So, supporting cancer patients who smoke to quit is important, but relapse rates are high (Hawari et al 2022). Concentrating on the psychology of quitting, "studies have indicated that confidence in ability to quit and belief that smoking contributed to the cancer's occurrence or prognosis were associated with readiness to

[5] About two-thirds of cancer survivors continue to smoke, and around one-quarter use e-cigarettes (Bjurlin et al 2022a).

quit. Conversely, perceived difficulty to quit, distress, and hopelessness were associated with continued smoking or relapse" (Hawari et al 2022 p2).

Hawari et al (2022) reported a study from the largest cancer centre in Jordan with 350 patients (104 former and 246 current smokers) between 2018 and 2020. A questionnaire was designed covering factors involved in behaviour change.

All participants agreed that quitting was important, but current smokers were significantly less confident about achieving it than ex-smokers. In terms of similarity between the two groups, "[R]oughly 31% of subjects believed smoking harms were exaggerated. Approximately 58% believed that an unhealthy lifestyle could cause disease, and approximately 59% reported disliking smoking despite being (or having been) smokers. About a third of subjects did not perceive smoking to be an addiction" (Hawari et al 2022 p3). Current smokers were more likely to be around other smokers, which made quitting difficult. Many patients "appeared to underestimate or lack knowledge about the value of procedural skills and small but critical steps such as avoiding smoking areas, removing visual triggers such as ashtrays, and avoiding situations that could trigger smoking" (Hawari et al 2022 p5).

The researchers concluded: "Jordanian cancer patients who smoke present with limited knowledge about the quitting process. Even when some success is observed, low rates of utilisation of specific quitting strategies were observed, highlighting the need for better counselling about quitting" (Hawari et al 2022 p1).

Bjurlin et al (2022a) analysed US data from the 2015-2018 "National Health Interview Survey" covering nearly 13 000 adults with a history of cancer. Among individuals with tobacco-related cancer, 18% currently smoked compared to 9.6% for non-tobacco-related cancer survivors, and the prevalences for e-cigarettes were 2.7% and 1.6% respectively. Dual use of cigarettes and e-cigarettes was similar among both groups (around 9%).

"Survivors of tobacco-related cancers have a higher prevalence of current cigarette smoking and e-cigarette use compared to survivors of non-tobacco related cancers. There was a sequential increase in the prevalence of cigarette use during each subsequent year from the time of a new cancer diagnosis, underscoring the need for long term tobacco cessation support among newly diagnosed adults with cancer" (Bjurlin et al 2022a p1).

Bjurlin et al (2022b) theorised that the continued use of e-cigarettes "may be driven by underappreciation of the harms and health implications of e-cigarette use (appendix 2A). Cancer survivors have different perceptions of risk compared to non-cancer participants and this plays a critical role in decisions to use tobacco and potentially e-cigarettes. The increase in e-cigarette use among cancer survivors may reflect a perception that e-cigarettes are low risk even though e-cigarette use has been linked to the potential of several smoking related malignancies" (p2).

US data from the "Health Information National Trends Survey" (HINTS) (2017-2019) were analysed by Bjurlin et al (2022b) in relation to this issue. The key question was: "Compared to smoking cigarettes, would you say that electronic cigarettes are: (1) much less harmful; (2) less harmful; (3) just as harmful; (4) more harmful; (5) much more harmful" (p2).

Nearly 12 000 respondents were included, of which 26.6% reported a history of cancer. The two groups were compared (cancer vs no cancer): there was no difference in numbers perceiving e-cigarettes as harmful or more so than tobacco cigarettes in both groups (around 70%).

Bjurlin et al (2022b) explained the findings thus: "Emerging data has recently highlighted the association of e-cigarette use with nicotine dependence and abuse liability, pulmonary injury and cardiovascular disease, along with potential risks for malignancy, which may be reflected in respondent's perception of increased harm. Furthermore, recent FDA [Food and Drug Administration] warnings regarding e-cigarette use and regulation of e-liquid in conjunction with changes to state laws may have heightened the awareness of the potential risks of e-cigarettes. The exponential growth in the number of e-cigarette research studies, cohorts with longer longitudinal follow up, as well as media campaigns, and public health commentaries, may have also contributed to the perceived harm among our study respondents" (p5).

2.3. SECOND PRIMARY CANCER

Secondary primary cancer (SPC) is "a new primary cancer that is not a recurrence or metastatic deposit of the initial lesion" (Phua et al 2022 p1). SPCs are more fatal than the first primary cancer (approximately twice as high cancer-specific mortality) (Phua et al 2022).

The causes of SPC are relatively unknown, but underlying genetic and lifestyle factors appear key.

Treatment for the first cancer (ie: radiotherapy and chemotherapy) are not viewed as important causes (Phua et al 2022).

Phua et al (2022) performed a literature review on cigarette smoking and SPC, finding twenty-one relevant studies published before March 2021 (of which eleven were cohort studies and ten case-control studies). "There was marked heterogeneity in methods used in terms of classification and timing of smoking, confounders adjusted for and duration of follow-up across the studies. Nine cohort and seven case-control studies classified smoking habits prior to diagnosis of first cancer while the remaining studies classified post-first cancer smoking habits" (Phua et al 2022 p1). Different classifications of smoking status (eg: how long since last cigarette before ex-smoker), cigarettes smoked per day, and pack-years of smoking were found, along with differences in the follow-up period, when quitting occurred (eg: pre- or post-diagnosis of first cancer), and the definition of SPC and cancer sites. Self-reported number of cigarettes smoked was the common measure, and under-reporting is a concern with this method (Phua et al 2022).

So, a meta-analysis was only possible with data from six studies, and this showed an increased risk of smoking-related SPC for former and current smokers compared to never smokers. "In conclusion, there was evidence that smoking might increase the risk of SPC in cancer survivors" (Phua et al 2022 p1).

2.4. ADVICE FROM HEALTH PROFESSIONALS

Smoking cessation counselling is recommended for cancer patients who smoke, but not all health professionals provide such advice. US data showed that individuals with tobacco-related cancer were more likely to receive advice than non-tobacco-related cancer patients, and healthy smokers (Matulewicz et al 2022).

This finding came from an analysis of the "Population Assessment of Health and Tobacco" (PATH) study (2017 wave). From a nationally representative sample of nearly 34 000 adults, 9915 self reported as current smoker, and overall 57% of them had been advised to quit by a healthcare professional in the previous year. Dividing the smokers in three groups - no cancer, non-tobacco-related cancer, and tobacco-related cancer - those advised to quit were 56%, 63%, and 73% respectively. Advice to quit is associated with the use

of evidence-based pharmacotherapies both in this study and in previous work (eg: Gallaway et al 2019).

Receiving a recommendation to quit from a healthcare professional has been found to be more effective in a review of over twenty-five trials (Stead et al 2013): 8% successful cessation rate vs 4.8% for those with no recommendation (Matulewicz et al 2022).

In a study of US oncologists, 61% reported providing smoking cessation advice (Ganz et al 2006), while in a survey of nearly 700 Australian medical and radiation oncologists in 2016 (Day et al 2018), only 2-3% managed smoking cessation efforts, and the remainder preferred other health workers to run such programmes (Stewart et al 2022).

The "Clinical Oncology Society of Australia" adopted a resolution in the mid-2010s to upskill all clinical staff around tobacco cessation, and to introduce an automatic referral to programmes like "Quitline", which patients had to opt out of (rather than opt in). "Early pilot work shows that people newly diagnosed with cancer who smoke and who were advised at that time to quit increased from 55% in 2016 [before the implementation] to 72% in 2019 [after]" (Stewart et al 2022 p1).

Smoking cessation programmes for hospitalised cancer patients are rare as most interventions are outpatient-based, but there is potential as a "teachable moment" (Stewart et al 2022), as Neerukonda et al (2022) showed. They analysed data from "UKanQuit", which trained staff in the USA to provide bedside tobacco treatment, including behavioural strategies, nicotine replacement, and post-discharge follow-up. The main outcome measure was self-reported abstinence for the past week when contacted six months after hospital discharge. The sample was 407 adults between July 2018 and October 2019.

Approximately one-third of the sample agreed to cessation intervention during hospital stay or at discharge, and/or referral to "Quitline". One hundred and fifty-one of these patients were reached at six months, and 29% reported abstinence.

This figure is similar to Griebel et al (1998) with a nurse-managed intervention, which found a biologically-verified 21% abstinence at six weeks post-discharge, while Stanislaw and Wewers (1994) reported 43% abstinence at five weeks post-discharge with a high-intensive intervention. Neerukonda et al (2022) commented: "Our study employed a minimal intervention similar to Griebel's but incorporated dedicated counsellors rather than nursing staff. We followed a large number of

patients over an extended period of time. Our finding that high rates of patients engaged in quit attempts suggests that hospitalisation is a good time to engage patients with cancer in tobacco treatment. We believe using both a high-intensive program and trained counsellors rather than medical staff will provide more adequate treatment and higher quit rates" (p3). Note that there was no control group in the Neerukonda et al (2022) study, and only self-report measures of smoking cessation.

In the USA, as part of the "National Cancer Institute (NCI) Cancer Moonshot programme", a point of care tobacco treatment programme was introduced called "Electronic Health Record-Enabled Evidence-based Smoking Cessation Treatment" (ELEVATE). Craig et al (2022) reported implementation at a cancer centre in St Louis, Missouri, in June 2018. All clinical staff at 21 oncology clinics were involved in routine tobacco treatment.

ELEVATE involves the stages of "assessment (asking patients about smoking status), provide a scripted brief advice to quit smoking, and discuss treatment options (medication and counselling)" (Craig et al 2022 p2).

Craig et al (2022) assessed outcomes at the St Louis centre pre-implementation (January-May 2018), and at five times between June 2018 and December 2020. The outcome of smoking cessation was 12% pre-implementation, but increased to 21% after implementation (though the covid-19 pandemic impacted the programme).

2.5. SCREENING

Lung cancer screening offered to smokers has the potential to reduce smoking rates. Heiden et al (2022) showed this with US data. The data came from the "Behavioural Risk Factor Surveillance System" (BRFSS) 2017-2020, which involved over 400 000 adults annually surveyed about health issues. The "United States Preventative Services Taskforce" in 2013 recommended lung cancer screening for individuals aged 55-80 years old (current or recent smokers) with ≥30 pack-year history.

In total, 12 382 participants were eligible for screening, but only 16% had taken up the offer. Comparing the screened and not screened, the former group were more likely to report a cessation attempt in the past year, and were less likely to be a current smoker.

The researchers concluded: "Better implementation of lung cancer screening programs is critical and may

profoundly increase smoking cessation in this population at risk of developing lung cancer" (Heiden et al 2022 p1).

In terms of causation, other studies (eg: randomised controlled trials) show that lung cancer screening "can improve smoking abstinence, though the direct effect of lung cancer screening on smoking behaviour may be minimal and rather reflect contextual advantages of frequent healthcare encounters" (Heiden et al 2022 p3).

2.6. UNHEALTHY BEHAVIOURS

Tobacco smoking is prevalent with head and neck cancer (HNC) patients, but self reports of cessation are not necessarily accurate (McCarter et al 2022). For example, Warren et al (2012) found that over a quarter of fifty patients undergoing treatment who self-reported no tobacco use were still smoking according to biochemical measures (table 2.1).

Other risk factors cluster with smoking, including alcohol use (appendix 2B), depression, poor nutrition, and lack of physical activity. These behaviours impact the outcome of treatment for cancer patients, particularly with HNC (McCarter et al 2022).

- Concentrating on genito-urinary (GU) cancers, Zhao et al (2022) raised the concern that smoking-related data is rarely collected and reported in oncology clinical trials.

- These researchers performed a literature review on smoking status data in clinical trials in GU oncology. Of the 354 relevant studies (published between May 2010 and May 2020) found, 92% did not report any details about the smoking status of the participants in the trial. "No studies used a validated measurement instrument or reported change in participants' smoking status over the study period. Absence of the collection and reporting of smoking-related data precludes further study of how smoking impacts outcomes and highlights an important deficiency in GU oncology clinical trial design" (Zhao et al 2022 p1).

- Zhao et al (2022) accepted that "only thirty scientific journals were included in our search of clinical trials. However, these journals represent the most likely avenue for publication of landmark and impactful genitourinary cancer trials" (p2).

Table 2.1 - Smoking status.

McCarter et al (2022) surveyed a sample of ninety-nine Australian HNC patients about different health behaviours over a three-month period during radiotherapy. Smoking was measured by self-report, and carbon monoxide concentration in breath. Other measures included alcohol use, depression and anxiety, food eaten, and physical activity.

Prevalence of smoking was self-reported at 4-7% during the study period, but biochemically verified at 13-29%. Hazardous drinking (based on "Alcohol Use Disorders Identification Test-Concise"; AUDIT-C score; Bush et al 1988) increased over time as did depression score. Healthy eating, and physical activity were both low. "The sub-group analysis of smokers (self-report) at long-term follow-up found no statistically significant differences in other health factors to non-smokers at long-term follow-up" (McCarter et al 2022 p2).

2.7. APPENDIX 2A - VAPING

Vaping carries some risks but is less harmful than smoking (table 2.2). However, misperceptions of the health harms of vaping are increasing in many countries" (East et al 2026 p9). These authors investigated harm perceptions of (nicotine) vaping. Perceiving vaping as harmful as smoking could discourage cigarette smokers to switch as a way of quitting cigarettes.

- The leader (2023) described the growth of vaping in recent years as "a global experiment with an imperfect smoking cessation device" (p5). The move from tobacco smoking to vaping is positive for individual health, but there is fear of the opposite, particularly among young people. It has been estimated that 7.5% of the populations of England and the USA vapes, but this is nearer to one-third among teens and young adults (Lawton 2023).

- In terms of health impacts, evidence is emerging of short- and long-term consequences. For example, the ingredients of the e-liquid - nicotine, and common solvents. The latter can "irritate and inflame the airways" (Lawton 2023 p32). While there are flavourings and sweeteners, which heat can change into different compounds (eg: reactive aldehydes) (Lawton 2023).

- Other risks are unintentional byproducts (eg: heavy metals released by the heating element), and the content of vape aerosols (eg: carbon monoxide; volatile organic compounds) (Lawton 2023).

Table 2.2 - Health concerns of vaping.

Three reviews on the subject were noted by East et al (2026):

i) Erku et al (2021) - 31 experimental and cross-sectional studies from the UK and the USA.

ii) Mylocopos et al (2023) - 39 studies of young people (mostly from the USA).

iii) Aly et al (2022) - Twenty studies (half from the USA).

East et al's (2026) review focused on interventions to change vaping harm perceptions, and whether harm perceptions predict vaping and smoking behaviour. Eighty-five relevant studies published between 2007 and 2023 in English, French or German were found.

1. Interventions to change vaping harm perceptions

Fourteen articles were found for young people (18 years and younger) and 32 articles on adults. A variety of interventions were involved, including educational workshops and programmes in schools, for example, and mass media campaigns. Generally, the interventions increased perceptions that vaping was harmful to health, and addictive (absolute harm), but also the misperception that vaping was as harmful as smoking (relative harm).

2. Harm perceptions and subsequent behaviour

Thirty-nine articles were found covering both young people and adults on this topic. Overall, there was some evidence that "both absolute and relative harm perceptions predicted vaping and smoking behaviours, such that perceiving vaping as harmful deterred vaping among both young people (8/9 studies) and adults (4/7 studies), while misperceiving vaping as equally/more harmful than smoking prevented adults from quitting smoking (5/6 studies)" (East et al 2026 p9).

In conclusion, interventions to change vaping harm perceptions could be effective, but care needs to be taken not to produce misperceptions of the harm which may discourage smokers from changing from cigarettes to vaping.

The methodological quality of the studies in the review varied, particularly the content of the

interventions, and the measures of harm perception.

The USA was the country of most studies, and researchers explained that it has "a unique e-cigarette regulatory environment (eg: no legal nicotine concentration limit on vapes and flavour restrictions in certain states) and generally negative health messaging around vaping, and articles spanned multiple years during which the US regulatory environment changed (eg: the age of sale increased from 18 to 21 years in 2019)" (East et al 2026 p39).

Another issue was that "most intervention evaluations were limited in only assessing perceptions before and immediately after the intervention and in a controlled experimental setting. Additional research is required to assess whether the changes in perceptions are sustained in the long term. Further, in the real world, exposure to information about vaping is more complex; for example, websites/social media are the most commonly cited source of vaping communication efforts among youth, and vaping campaigns on social media are often accompanied by counter arguments and public reactance, which may weaken the impact of the intervention" (East et al 2026 p39).

2.7.1. Packaging

Packaging is an important element in the attraction of vaping particularly to youth. "From being visually appealing in shops (point of sale), to featuring in online advertisements and social media campaigns, packaging is key to brand identity and promotion. As well as bright colours, it is commonplace for brands to also use youth-appealing elements, such as images, cartoon characters, stylised fonts, and novel brand and flavour names on vapes and e-liquid packaging. The packaging of vapes influences the appeal of vaping products to youth and young adults, and both youth and adults report that reducing bright colours and branding features would make vapes less appealing to youth" (Taylor et al 2025 p2). Flavour is another important element.

Taylor et al (2025) investigated vape packaging designs and attractiveness to youth in an experimental study. Participants were presented with one of four packages - branded, white with usual text, white with brief flavour descriptor (eg: raspberry), or white with coded flavour descriptor (eg: FR248). The participants were recruited from the "Action on Smoking and Health 2024 Smokefree Great Britain Youth Online Survey" (ASH-

Youth) (over 2700 11-18 year-olds), and an online sample of adults (nearly 4000). The outcome measure was "no perceived interest in trying vape".

No perceived interest in trying was lowest for branded products, particular for youth. Branded packaging is attractive to teenagers, and so making the packaging plain would reduce the appeal. "Overall, findings support policies to regulate vape packaging", ended Taylor et al (2025 p11).

2.7.2. Swap to Stop

The UK Government introduced the "Swap to Stop" programme in 2023. It involved a free vape starter kit and behavioural support for smoking cessation (Buss et al 2026).

Buss et al (2026) reported an evaluation of the programme after one year using data from the "Smoking Toolkit Study" 2021 to 2024. This involved telephone interviews with approximately 2500 adults in the UK each month.

Concentrating on England only, it was found that "the introduction of Swap to Stop in December 2023 was associated with a 1.5 absolute percentage point increase in the proportion of people in England using vapes in past-year quit attempts that persisted to December 2024... The introduction of Swap to Stop (which provides free vape starter kits with behavioural support to quit smoking) in England appears to be associated with a statistically significant increase in quit attempts using vapes" (Buss et al 2026 p1). This translated into 125 000 additional quit attempts using vapes attributable to "Swap to Stop".

The researchers commented: "Although the overall effect observed in this study may appear modest, even small treatment effects for smoking cessation are clinically meaningful because the health benefits of quitting smoking are enormous. However, it is also noteworthy that some of these additional 125 000 quit attempts may have occurred regardless of Swap to Stop, albeit potentially unaided or with less effective methods. It is also unclear how many of those who attempted to quit might (i) have started using vapes alongside cigarettes; (ii) switched completely from smoking to vaping; or (iii) only vaped in the short-term until they completely stopped using nicotine altogether" (Buss et al 2026 p6).

The study had the outcome measure of use of vapes to

quit attempts, not successful quitting. Also it was not possible to distinguish the benefits of vapes from behavioural support as "Swap to Stop" involved both together. Furthermore, the programme included collaboration with job centres, homeless centres, and social housing providers, for instance, as well as NHS services.

In terms of previous research, vapes are more effective than nicotine replacement therapy in smoking cessation generally, while an assessment of a pilot study of "Swap to Stop" in 2018 in a socially deprived area of England reported that 37% had quit cigarette smoking at four weeks follow-up (Buss et al 2026).

APPENDIX 2B - ALCOHOL CONSUMPTION

Alcohol is viewed as a "leading modifiable risk factor" for a variety of different cancers, but its consumption remains high (Abraham et al 2025).

But how does drinking frequency and quantity influence cancer risk? Abraham et al (2025) reviewed the evidence with particular reference to US adults. The researchers found sixty-two relevant studies published up to June 2025. The majority of the studies were cohort studies (n = 45) (ie: longitudinal).

Alcohol consumption was consistently identified as a risk factor for breast, colorectal, and liver cancers in particular, and higher frequency and/or greater quantity of alcohol consumed were key. "Dose-response relationships were a common finding, underscoring that risk is not limited to heavy or chronic use; even moderate levels of intake were linked to increased risk for certain cancers" (Abraham et al 2025 p52).

Cancer risk was increased for excessive alcohol consumption by older adults generally, all adults depending on the type of cancer, individuals with socio-economic disadvantage, and those with a family history of cancer. "Racial and ethnic differences in alcohol-attributable cancer rates are well-documented and may be driven by a combination of biological predispositions (eg: ALDH2 polymorphisms in East Asian populations) and challenges with affording costs of healthcare services, cancer screening, and early treatment" (Abraham et al 2025 p52).

Daily or near-daily alcohol consumption, even at moderate levels, was a greater risk than occasional drinking. Co-morbidities like obesity and diabetes increased the cancer risk.

In terms of the biological pathways from alcohol consumption to cancer, several have been proposed: "Ethanol metabolism produces acetaldehyde, a genotoxic compound that can damage DNA and impair DNA repair mechanisms. Alcohol also increases oestrogen levels, contributing to hormone-sensitive cancers such as breast cancer. Additional mechanisms include oxidative stress, immune suppression, and facilitation of carcinogen absorption. These mechanisms may interact with pre-existing co-morbidities, lifestyle factors, and genetic predispositions to accelerate cancer initiation and progression" (Abraham et al 2025 p53).

Commenting on the methodology of the studies in the review, Abraham et al (2025) noted that controlling for confounders was not always the case: "Although several studies reported adjusting for confounders established in the literature as commonly associated with the relationship between alcohol intake and cancer, such as age, sex, smoking status, dietary factors, body mass index (BMI), physical activity, and family history of cancer, some did not consistently adjust for all relevant confounders. For example, some studies controlled only for age and sex, while others lacked adjustment for smoking or dietary factors, which may have introduced residual confounding" (p53). Also self-reports of alcohol consumption were prone to recall bias, and differences in quantity classification (eg: a "glass" of wine can mean different volumes) (Abraham et al 2025).

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3. BREAST CANCER

3.1. Diet
3.2. Anti-psychotic medication use
3.3. Mammography screening
3.4. Appendix 3A - Vegetarian diet and cancer
3.5. Appendix 3B - Obesity and cancer
3.6. References

3.1. DIET

In 2023 there was an estimated 2.3 million new female breast cancer cases globally, and 764 000 deaths. Between 1990 and 2023 the number of new cases increased by 16%, but the resulting deaths fell by 5%. But both new cases and deaths increased most in low-income countries during this period. "The stable incidence and declining mortality rates of female breast cancer in high-income nations reflect success in screening, diagnosis, and treatment. In contrast, the concurrent rise in incidence and mortality in other regions signals health system deficits" (GBD 2023 Breast Cancer Collaborators 2026 p302).

Poor diet, tobacco use, and high blood sugar level were the most common risk factors, but alcohol use, and tobacco had declined in importance in the last thirty years (GBD 2023 Breast Cancer Collaborators 2026).

The link between consumption of meat and breast cancer risk is becoming increasingly discussed. There is research on diet generally and both breast cancer risk and recurrence. Epidemiological studies have shown that being overweight is associated with increased risk of breast cancer in healthy women, while improving diet for breast cancer patients reduces recurrence risk in some studies (Berrino et al 2024) (table 3.1).

The DIANA-5 (DIet and ANdrogen) trial was set up to assess the impact of a diet based on Mediterranean and macrobiotic components with breast cancer patients. Over 1500 women with a high risk of recurrence were randomly assigned to the active dietary intervention (eg: active support to cook healthy meals; regular joint meals) or a control group (general recommendations) between 2008 and 2012 in Italy. Follow-up lasted five years (Berrino et al 2024).

There was no difference in the number of women with breast cancer recurrence between the two groups. However,

STUDY	FINDING
Nurses' Health Study (Kim et al 2011)	No significant association between Mediterranean diet and breast cancer-specific mortality, but a reduced risk of non-breast cancer mortality
EPIC Study (Castro-Espin et al 2023)	As above
Women's Intervention Nutrition Study (WINS) (Chlebowski et al 1992)	Reduced fat intake and calories and a significant reduction in recurrence of breast cancer, specifically oestrogen receptor-negative tumours
Women's Healthy Eating and Living (WHEL) Study (Pierce et al 2007)	Reduced fat and calorie intake, and increased fruit, vegetables, and fibre; no significant association found with recurrence

Table 3.1 - Four key studies on diet improvement and breast cancer recurrence.

comparing the most and least compliant tertile in the diet group (as self-reported) showed a benefit (Berrino et al 2024).

Michelle Harvie of the "Prevent Breast Cancer Research Unit" at the University of Manchester noted that "red meat does not screech out of the research for breast cancer in the same way as it does for bowel and heart health" (quoted in Rumbelow 2026) (appendix 3A). Smoking, drinking, and obesity (appendix 3B) are stronger risk factors in breast cancer (Rumbelow 2026).

The type of breast cancer is also relevant. High vegetable consumption reduced the risk of oestrogen receptor-negative breast cancer, but not the oestrogen-positive kind (Jung et al 2013). High consumption translated into 400 g or four servings per day (Rumbelow 2026).

Anderson et al (2018) found that the risk of cancer was increased only for post-menopausal women, and only for processed (not unprocessed) red meat (Rumbelow 2026). This finding came from the UK Biobank cohort (over 260 000 women aged 40-69 years at recruitment).

3.2. ANTI-PSYCHOTIC MEDICATION USE

A South Korean population-based cohort study found a link between long-term use of anti-psychotic medications by women diagnosed with schizophrenia and breast cancer risk (Yang et al 2025). The relative risk was increased

by 25% compared to the general population, and the longer the use of anti-psychotics the greater the risk. "First-generation", but not "second-generation" anti-psychotics were the problem (Corbeil et al 2026).

The anti-psychotics that increased prolactin were the concern, whereas prolactin-sparing anti-psychotics were not a risk (Corbeil et al 2026). This is supported by data from Finland (Taipale et al 2021), and Sweden (Solmi et al 2024). "Altogether, these studies and the findings by Yang et al hint that hyperprolactinaemia induced by these medications contributes to the development of breast cancer" (Corbeil et al 2026 p7).

These findings came from real-world observational studies not randomised controlled trials (RCTs). "Although RCTs are the gold standard for establishing causality, their stringent exclusion criteria in schizophrenia studies, for example, often exclude participants with co-morbidities commonly observed in people with the condition, limiting the generalisability of their findings to clinical practice. Real-world studies address this gap by including diverse populations and capturing long-term outcomes, including rare or delayed adverse effects that often go undetected in RCTs. For instance, breast cancer risk has not been identified in RCTs of anti-psychotic maintenance treatment, likely because of their duration, which in most cases does not exceed 52 weeks. Given that the latency period for drug-cancer associations is typically at least 1–5 years, detection of many such risks requires extended follow-up" (Corbeil et al 2026 p7).

But, Corbeil et al (2026) accepted, "real-world studies also have limitations, particularly the lack of randomisation, which makes them more susceptible to confounding arising, for example, from unmeasured behavioural, genetic or environmental factors. Factors that may confound the association between anti-psychotic use and risk of breast cancer are not captured in most population registry-based real-world studies, including genetic predisposition, prolactin serum concentrations, illness severity, treatment adherence, access to care, breast cancer screening and lifestyle" (p8).

Corbeil et al (2026) ended by commending the use of real-world studies to "inform clinicians about the safety and effectiveness of interventions across diverse populations and help identify which patients are most likely to benefit from specific treatments" (p9).

3.3. MAMMOGRAPHY SCREENING

Mammography screening has been found to reduce the average risk of female breast cancer mortality (BCM) by 20-35%, but screening may not be as effective in detecting relapses earlier in breast cancer survivors (BCS) compared to the general population (Sardini et al 2025).

Sardini et al (2025) analysed data from Funen in Denmark for the period 1993 to 2007 for BCS invited to a screening programme (study group) and compared them to BCS in other parts of Denmark with no screening programme (control group). The screening was biennially for 2109 50-69 year-olds, of whom 406 (19%) died during the study period. This compared to 3385 deaths (22%) of the 15 417 women in the control group. The BCM relative risk among screened BCS was less than the non-screened survivors (10-12% less), but this reduction in risk was lower than the benefits of screening for the general population (22-37% reduction in relative risk in other Danish studies of the same age group; eg: Olsen et al 2005). The researchers felt that the explanation was that BCS uptake of screening was low. They concluded that increasing participation rates in screening survivors was crucial. "Mammography screening seems to be an effective screening method for those survivors who do participate" (Sardini et al 2025 p5).

This study used retrospective, secondary data, though the quality of official Danish health records is "very high" with only small inaccuracies (Sardini et al 2025). The time to screening after diagnosis for BCS was an average of 8.7 years, while today in the national screening programme in Denmark it is recommended to be three years. The data analysed from the county of Funen was pre-national screening (introduced in 2008-2010; Sardini et al 2025).

Gommers et al (2026) reported the first randomised controlled trial on the use of AI in mammography screening. The AI-supported software was trained on over 200 000 mammography scans to rank the likelihood of cancer being present.

Using data from over 100 000 women in Sweden, the analysis of the mammogram was performed by two radiologists, or AI-supported software (and then radiologists). Women in the latter group were 12% less likely to develop "interval cancer" (rapidly growing tumours between screenings) than the human-only analysis group (Wong 2026). "The improvement may be because the AI

is better able to detect cancers at an early stage. So, while radiologists might overlook small tumours that would develop into an interval cancer, the AI can spot them" (Wong 2026 p7).

Previous research had found that AI-supported software detected around 30% more cancers than two radiologists, without an increased rate of false positives (Wong 2026).

3.4. APPENDIX 3A - VEGETARIAN DIET AND CANCER

In the late 19th century, "early though unsubstantiated claims were made that cancer is rare in vegetarians" (Dunneram et al 2026 pp1-2). This has led to an interest in the role of diet in cancer.

The "Cancer Risk in Vegetarians Consortium" brought together nine prospective studies from three continents to examine the relationship between vegetarian diets and cancer risk. In total, there were 1.6 million meat eaters, around 57 000 poultry eaters (but no other meat), approximately 43 000 pescatarians (fish eaters), over 63 000 vegetarians, and 8849 vegans. The average follow-up time was sixteen years.

"Compared to meat eaters, poultry eaters had lower risk of prostate cancer, pescatarians had lower risks of colorectal, breast and kidney cancer, vegetarians had lower risks of cancers of the pancreas, breast, prostate, kidney and multiple myeloma but higher risk of squamous cell carcinoma of the oesophagus, and vegans had higher risk of colorectal cancer" (Dunneram et al 2026 p1).

The classification of participants was based on self-reports of "typical diet" or food eaten in last 24 hours to twelve months, and there were slight differences in data collection between the studies (eg: number of food groups in food frequency questionnaire; time of data collection; resurveying). However, there was no significant heterogeneity between the cohorts for most associations between diet and cancer type (Dunneram et al 2026).

3.5. APPENDIX 3B - OBESITY AND CANCER

The "International Agency for Research on Cancer" classifies twelve cancers as obesity-related cancers (eg: colorectal; pancreas; oesophagus), but others may be obesity-related also (eg: prostate). "Body weight and metabolic syndrome are each independently associated with

higher rates of obesity-related cancers, with highest risk observed in patients with the metabolically unhealthy overweight/obese phenotype, which is defined as having a BMI greater than 25 and at least 1 component of metabolic syndrome: hypertension, dyslipidemia, or insulin resistance" (Shen et al 2026 pE2).

Cancers have ten acquired properties - "sustained proliferation, unlimited cell division, resisting cell death, evading growth suppressors, angiogenesis, activating invasion and metastasis, modified energy metabolism to support cellular proliferation, evading immune destruction, genomic instability, and inflammation" (Shen et al 2026 pE2). How does obesity affect these properties and so promote cancer growth?

Shen et al (2026) offered an answer based on a review of current knowledge: "Obesity and overweight are characterised by excess accumulation of adipose tissue, which disrupts its primary function of energy storage. Excess energy, in the form of free fatty acids, is transferred to developing cancer cells and stimulates cancer development through genomic instability caused by oxidative stress and DNA damage. Other defining features of adipose tissue dysfunction include inflammation and altered hormone production such as increased oestrogens and leptin and decreased adiponectin. Inflamed adipose tissue is associated with systemic elevations in inflammatory mediators..." (pE1).

On the positive side, weight loss of more than 10% of body weight produces "modest reductions in obesity-related cancer incidence" (eg: up to 0.05% reduction) (Shen et al 2026 pE1). While Wang et al (2024) found that patients with type 2 diabetes taking GLP-1 receptor agonists (compared to insulin) had lower risk of obesity-related cancers. This was a retrospective study of 1.6 million US patients' electronic health records (Shen et al 2026).

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4. COLORECTAL CANCER

4.1. Early onset colorectal cancer
4.2. Aspirin use
4.3. Diet
4.4. References

4.1. EARLY ONSET COLORECTAL CANCER

In recent years the number of cases of cancer among younger adults (under 50s) has been rising, especially colorectal cancer. Early-onset colorectal cancer (EOCRC) (diagnosis before 50 years old) is over 10% of all new cases globally (of 1.9 m in total in 2022), with predictions of further increases to come (Lawton 2025).

The increase in EOCRC was first noticed in 2003 in an analysis of US data for 1973 to 1999. These data showed at the same time that cases in the over 60s were stable or falling (due in part to screening programmes for older individuals). Increases in the 20-40 year-olds have also been seen in other high-income countries, and elsewhere (Lawton 2025).

More specifically, based on data from a large cancer centre in northwest England for the period 2013 to 2021, Angelakas et al (2024) found a significant increase in EOCRC cases. There were 37 cases in 2018-19, which increased to 118 cases in 2020-21. The researchers concluded from their sample: "EOCRC has distinct characteristics, including predominantly left-sided tumours, advanced disease at diagnosis, and aggressive pathology" (Angelakas et al 2024 pe1689).

The question is why is colorectal cancer increasing in the under 50s. Environmental and/or lifestyle explanations are attractive. For example, consumption of highly processed, low-fibre foods, red meats, and alcohol increased during the lifetime of under 50s, with the subsequent rise in obesity and health-related conditions. Other possibilities are the high use of anti-biotics and their impact on the gut microbiome, and the lack of physical activity (Lawton 2025).

Angelakas et al (2024) reviewed the evidence on potentially modifiable risk factors for EOCRC. Increased risk was associated with a diet rich in red and processed meat, high consumption of sugar-sweetened beverages, anti-biotic exposure, and sedentary behaviour. Risk was reduced by high vegetable and fruit consumption, and greater vitamin D intake. There was no relationship for

high fibre intake. The eleven studies quoted varied in size and methodology, and a number of them showed no statistically significant association. Clear risk factors for younger generations and EOCRC are not well established at this stage (beyond the general risk factors for colorectal caner).

An alternative view is that EOCRC may be a different disease to late-onset colorectal cancer (LOCRC). Potential differences include that LOCRC tends to be found on the right side of the bowel and EOCRC on the left (ie: different tissue types), and that LOCRC is adenocarcinoma type of cancer compared to neuroendocrine tumours with EOCRC (Lawton 2025).

Comparing 759 patients with EOCRC and 687 patients with average-onset, Cercek et al (2021) noted that the two cancers were "clinically and genomically indistinguishable", apart from EOCRC being "more commonly left-sided and present with rectal bleeding and abdominal pain" (p1683). The patients attended a cancer centre in New York between 2014 and 2019.

4.2. ASPIRIN USE

Aspirin as a "wonder drug" for colorectal cancer (CRC) has emerged after a study in Melbourne, Australia (Kune et al 1988) found a reduced risk. Subsequent studies have found mixed results (MacRae 2025).

Sikavi et al (2024), for example, analysed over thirty years of US data for over 107 000 adults who self-reported aspirin use. At least two tablets per week could reduce the risk of CRC, but mainly for those individuals with the unhealthiest lifestyles (higher body mass index, higher smoking and alcohol intake, poor diet, and least exercise) (MacRae 2025).

Aspirin appears to help in terms of recurrence when the CRC is caused by a specific genetic mutation related to the PI3K signalling pathway (Martling et al 2025). While a study with mice found that metastasis was reduced with aspirin use as there is increased immune functioning (Yang et al 2025).

The use of aspirin is studied in two main ways - as a prevention of cancer, and as a treatment for individuals after diagnosis. Concentrating on CRC and the latter, Madge et al (2022) observed: "It is unclear whether the outcome depends on the time of starting aspirin, ie: comparing patients who were taking aspirin

before their diagnosis for other reasons (eg: cardiovascular risk factors) and continued afterwards (primary prevention of CRC combined with tertiary prevention) with those who only began taking aspirin after their diagnosis of CRC (tertiary prevention). Furthermore, it is not clear whether certain gene expression types have an influence on the outcome of CRC" (p1408).

Madge et al (2022) performed a meta-analysis and review of the survival benefit of aspirin plus standard care versus standard care in patients with CRC. Twenty-seven relevant studies were found (published before mid-2019), of which 25 were cohort studies. The distinction was made between individuals taking aspirin before their diagnosis ("pre-diagnosis" group), and those who used aspirin after diagnosis of CRC ("post-diagnosis" group).

Overall, mortality was reduced by aspirin use with standard care, though this varied with specific gene expression type (eg: high expression of PTGS2 and longer survival). There was limited difference in survival benefit between pre- and post-diagnosis aspirin use.

The aspirin dosage varied between studies, and there was limited information about side effects, while the stage of CRC of participants at recruitment also varied. Most studies, however, were rated as good methodological quality.

More research, particularly randomised controlled trials, was one conclusion of the study (Madge et al 2022).

Other studies find benefits of aspirin use for some cancer types (eg: stomach), but rise the risk for others (eg: lung), and does not prevent remission in breast cancer (MacRae 2025). So, "the jury is still out on whether aspirin can reduce the spread of cancer in people" (Rahul Roychoudhuri, University of Cambridge, quoted in MacRae 2025).

4.3. DIET

There is some evidence that eating dairy foods reduces the risk of colorectal (or bowel) cancer, but the studies find correlations/associations and not causation (Simms 2025).

For example, the consumption of calcium (as found in dairy products) was key as a protective factor. Papier et al (2025) analysed data from the "Million Women Study" in

the UK [6] on 97 dietary elements. The data set included over 540 000 participants, of which over 12 000 were diagnosed with colorectal cancer over sixteen years of follow-up. Milk and dairy consumption was found to be inversely associated with risk of colorectal, colon, and rectal cancers. Also found was "a positive association with red and processed meat intake and weaker inverse associations with breakfast cereal, fruit, wholegrains, carbohydrates, fibre, total sugars, folate, and vitamin C" (Papier et al 2025 p1). Furthermore, alcohol increased the risk of these cancers.

Meanwhile consumption of two servings or more per week of yoghurts (which contain Bifidobacterium) and colorectal cancer incidence was shown in an inverse relationship by Ugai et al (2025). Tumour tissue was analysed for Bifidobacterium presence in 1121 colorectal cancer cases in a sample of 132 000 individuals. The data came from two ongoing US cohort studies - the "Nurses' Health Study" n = 121 700 women; started in 1976) and the "Health Professionals Follow-up Study" (n = 51 529 men; began in 1986). Consumption of yoghurt was measured at baseline as part of a food frequency questionnaire and then every four months approximately.

Concentrating on specific foods or nutrients and their relationship to cancer here is probably too simplistic as there is a "complex connection between our diet and cancer risk, with there being no shortcuts to health" (Simms 2025 p10).

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[6] Between 1996 and 2001 1.3 million women with an average age of 56 years in England and Scotland were invited for breast screening by the National Health Service and to join the study (Papier et al 2025).

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5. MISCELLANEOUS CANCERS

5.1. Prostate cancer
5.2. Ovarian cancer

5.1. PROSTATE CANCER

"The prostate gland is situated at the base of the bladder, and its basic function is to provide the seminal fluid that nourishes and supports spermatozoa in transit from the testicles during ejaculation. Cancers arise in the lining epithelium of the prostate gland: they range from low-grade tumours that require no treatment to rapidly growing, highly lethal cancers" (James et al 2024 p1684).

Prostate cancer risk increases with age, and so an ageing population will mean more cases. Predictions of 25% increases in cases and deaths in the rich countries in the next twenty years have been made (Lawton 2024). "The Lancet Commission on prostate cancer", which convened with multiple experts in the field, and as reported in James et al (2024), predicted that the number of new cases will rise annually from 1.4 million in 2020 to 2.9 million men (primarily due to a longer-living ageing population).

Other key points raised by the Lancet Commission included the disproportionate focus on (White) men in rich countries, while prostate cancer is rising especially in low- and middle-income countries (LMICs), and men of African heritage have increased risks. The lack of early diagnosis in LMICs was a particular concern. Issues around screening and treatment were noted along with the potential of technology to help, and the shortage of specialist medical staff (James et al 2024).

Three key recommendations of the Lancet Commission were presented (James et al 2024):

i) Clear diagnostic pathways with early detection, but not overdiagnosis, which include universal screening from 50 years old.

ii) The use of "novel methods of empowering patients" (James et al 2024 p1684) (eg: cloud-based medical record systems; AI).

iii) The "resource-sensitive guidelines should be implemented to maximise the effect of available therapies, especially surgery and radiotherapy, use of

which is often limited in LMICs" (James et al 2024 p1684).

"Unlike many other cancers, the risk of prostate cancer can't be significantly reduced by lifestyle changes or public health interventions. This makes the increase in the condition a different challenge from the inevitable rise in cancer overall as populations age" (Lawton 2025 p41).

One solution is early-stage intervention, which requires a universal screening programme for men above fifty years, say. But what method to use in such a programme? The prostate-specific antigen (PSA) test has been used for many years, but false positives and false negatives are a concern. A false positive is the test telling the man that they have cancer when a biopsy, say, shows that it is not so. There are consequences to an unnecessary biopsy (eg: infection; impotence). A false negative is the test giving the "all clear" impression, but having missed the cancer. While a true positive could be an "indolent" cancer, where growth is so slow that the man will not die from it (Lawton 2024).

Single PSA test-based screening programmes may produce no population level benefits (table 5.1). But regular testing over time could be beneficial.

- Ilic et al (2013) reviewed the evidence on prostate cancer screening, finding five studies, and concluded that "PSA screening led to an increase in prostate cancer diagnoses but did not reduce overall nor disease-specific mortality" (Ilic et al 2018 p2). Ilic et al (2018) updated this review, and ended up with five unique randomised controlled trials (reported in 32 articles) published before April 2018. The number of participants in total rose from 340 000 in Ilic et al (2013) to 720 000.

- The trials varied in screening frequency and interval, age of participants, screening methods, and PSA thresholds for biopsy. Consequently, Ilic et al (2018) concluded that "screening probably had no effect on all-cause mortality... and may have no effect on prostate-specific mortality" (p1). There was a small increased risk for negative consequences of unnecessary biopsys (eg: for every 1000 men screened, three extra would suffer urinary incontinence from subsequent biopsy).

Table 5.1 - PSA test screening.

In a longitudinal study with over twenty years of data ("Goteberg Randomised Population-Based Prostate Cancer Screening Trial"), regular PSA testing (every

second year) reduced prostate cancer mortality compared to controls (opportunistic screening), but the detection of new cases was higher in the screening group (ie: "high-risk of detecting small slow-growing cancers"; p292) (Franlund et al 2022). In December 1994 20 000 men born between 1930 and 1944 were randomly chosen from the Goteborg population in Sweden, and half of respondents were randomised to screening. Twenty-two years later, the screening group included 1528 cases of prostate cancer and 112 deaths compared to 1124 and 158 respectively in the control group.

Alternatively, the response to a positive test could be a MRI (magnetic resonance imaging) scan of the prostate gland, which has less risk than a biopsy, or "active surveillance" (ie: regular retesting).

Other possible biomarkers include kallikrein (a protein often elevated in prostate cancer), or genes (eg: a mutation of the BRCA2 gene associated with breast and ovarian cancer).

The "BARCODE 1" study was designed to assess genetic screening for prostate cancer, specifically a polygenic risk score (PRS). Male participants aged 55 to 69 years were recruited in 2019 in London and Southern England. No personal history of prostate cancer was a requirement.

Around 6400 men were genotyped, and 745 had a PRS above the 90th centile (which was used as the cut-off point). The PRS was calculated based on 130 risk gene variants (established from previous research), and DNA analysis was made on a saliva sample. Of the 745 high-PRS men, 468 accepted follow-up (MRI and biopsy), and 40% of them (n = 187) were found to have prostate cancer. Of these 187 cases, 21% (n = 40) were classified as high or very high risk, and 55% (n = 103) as "intermediate" risk.

It was estimated that 73 men were detected by the PRS who would have been missed by standard diagnostic programmes in the UK at that time. It was also calculated that 39 men with a PRS above the 90th centile would be "overdiagnosed" (ie: the prostate cancer would take longer than their remaining lifetime to progress to clinical cancer).

A PRS alongside established risk factors has potential was the conclusion.

Note that the sample was volunteers, of European ancestry, highly educated and largely from professional occupations, with a family history or interest in prostate cancer (McHugh et al 2025).

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5.2. OVARIAN CANCER

Survival rates after diagnosis between cancers vary (eg: 90% survive to five years with breast cancer compared to 50% with ovarian cancer) (Hodson 2021). In the USA, for example, breast cancer research has received nearly twenty times more government funding between 2007 and 2014 than ovarian cancer (Hodson 2021). This has led to ovarian cancer being described as "a hidden condition" (Hodson 2021) (table 5.2).

A new class of drugs has recently emerged that could "transform the treatment of ovarian cancer" (Makin 2021 pS36) - PARP inhibitors (poly(ADP-ribose) polymerase inhibitors). These drugs block enzymes involved in the DNA repair processes that cancer cells use during multiplying. This is exploiting the principle of "synthetic lethality" (Makin 2021) [7].

PARP inhibitors have been shown to be effective where BRCA gene mutations are the cause of the tumour (eg: Banerjee et al 2020), but to a lesser degree with non-BRCA mutation tumours (Makin 2021) (table 5.3).

[7] More technically, synthetic lethality is "a type of lethal cell interaction in which the co-occurrence of two events results in cellular death. Essentially, because of functional redundancy, cells can tolerate the loss of a single gene in isolation, but not the combined loss of the redundant genes or pathways. Redundant pathways allow the cell or organism to continue functioning and reproducing despite the failure of an important pathway. Synthetic lethality occurs when the primary and the redundant gene or pathway are inactivated: even though blocking only one of these pathways would not be lethal; the cell cannot survive the loss of both" (Abdullah 2021).

- In 2019 one-third of countries in the world did not have cancer registries (ie: national data on cases), and the "necessary data to inform policies" on ovarian cancer is even less (Fiscutean 2021).

- Western countries have higher rates of ovarian cancer than non-Western ones, but this is probably a product of data collection rather than actual differences. Comparisons between countries and regions, even so, is limited by the standardisation (or lack of) of data (eg: definitions; classifications) (Fiscutean 2021).

- High-quality registry data includes the number of cases at each stage of the disease, and this helps to understand early and late diagnosis and the survival rate. For example, five-year survival is around 90% with early detection (compared to around 10% with late diagnosis) (Fiscutean 2021) [8].

Table 5.2 - Lack of data.

- Stage of cancer of participants at start of trial.

- Type of cancer (eg: BRCA mutation).

- Specific drug or drugs used (eg: olaparib; oliparib and bevacizumab).

- Outcome measures (eg: progression-free survival at six months; prevention of relapse).

Table 5.3 - Key methodological differences between clinical trials of PARP inhibitors.

Data from the USA on ethnic differences show that Black women have lower survival rates and higher rates of recurrence/relapse than non-Hispanic White women. Furthermore, Black women are less likely to be recruited in PARP inhibitor trials (George 2021).

Whitmore et al (2020) found that Black women in the USA had a worse response to chemotherapy, even controlling for cancer stage, tumour grade, and treatment regimen. "The biological underpinnings of this are unclear, but genetics might play a part" (George 2021 pS39).

Differences have been found in vaginal microbiome between individuals based on ethnicity (eg: Fettweis et al 2014), while Nene et al (2019) showed an association

[8] A twenty year trial of ovarian cancer screening (based on a protein called CA125) (Menon et al 2021) surprisingly found no difference in number of deaths with early detection (Purcell 2021).

between ovarian cancer and an imbalanced vaginal microbiome in women under fifty years old. This was part of an attempt to establish the causes of ovarian cancer beyond genetic mutations, which explain only about one in ten of cases (Photopoulos 2021).

Establishing causation is the issue, however. "With the disease appearing later in life, and given the difficulty of carrying out large longitudinal studies, proving causation will be tough" (Photopoulos 2021 pS41). One theory is that certain bacteria in the vaginal microbiome that are harmful migrate to the ovaries and cause infection which is the basis of the cancer (Photopoulos 2021).

A certain version of the BRCA2 gene increases the risk of breast cancer three to five times and ovarian cancer 9-14 times compared to the general population (table 5.4). While individuals with a BRCA1 gene mutation have around a 40% risk of ovarian cancer in their lifetime compared to 1.2% in the general population. But 80% of ovarian cancer cases do not involve these genes (DeWeerdt 2021).

- To find those individuals with the BRCA gene variants, genetic testing holds potential. For example, high risk carriers could undergo prophylactic/preventive surgery to remove ovaries and fallopian tubes before tumours appear (Madhusoodanan 2021).

- "But this increased genetic risk does not mean that the disease is a certainty. Although clinicians make recommendations on the basis of biology and medical history, individual's choices depend on their own personal history of disease or risk tolerance" (Madhusoodanan 2021 pS51). For example, Hao et al (2020) investigated the response of 59 women who had been informed of carrying BRCA1 or BRCA2 gene risk variants, but had no history of cancer. About half visited a genetic counsellor within one year of receiving the news, while 12% of the total had their ovaries removed as prevention. Anecdotally, "people who have seen family members with advanced ovarian cancer are more likely to accept the idea of surgical prevention than someone who learns out of the blue that they carry a pathogenic BRCA1 variant" (Madhusoodanan 2021 pS51).

- Mutations in the BRIP1 gene, for instance, slightly increase the cancer risk, but in no way as high as the BRCA1 mutation. Should such women have preventive surgery?

- Genetic testing of women diagnosed with ovarian cancer in order to warn genetic relatives is another option. But only about one-third of US women take this option (though it is recommended for all those diagnosed with ovarian cancer) (Madhusoodanan 2021).

Table 5.4 - Genetic testing.

Ovarian cancer was assumed to develop from cells on the surface of the ovary by early physicians, and it was not until the end of the 20th century that fallopian tube tissue was implicated. "The fallopian tubes are not, however, the origin of all ovarian cancers. Certain rarer kinds of ovarian tumour seem to arise from the ovaries themselves or from other tissues" (DeWeerdt 2021 pS43).

Since the late 1990s the "winning combination" of treatment has been the drug paclitaxel, and the platinum-based chemotherapy cisplatin (Keener 2021). But 10-15% of tumours do not respond to cisplatin, and many tumours that initially responded, return as resistance is the problem (Keener 2021). Tumour cells can react to chemotherapy by enhancing DNA repair, making higher levels of molecular pumps to remove drugs, or producing proteins that remove the drug (Keener 2021).

Two issues are important - who will respond to chemotherapy, and finding alternatives to cisplatin. In the former case, tumours unable to repair themselves is a good indicator, while Hoppe et al (2021) reported that individuals with low levels of the protein RAD51 had better outcomes. "Platinum resistance is so hard to predict and treat because it has no single cause" (Anil Sood, US gynaecological oncologist in Kenner 2021).

Alternatives to cisplatin include paclitaxel and bevacizumab (a monoclonal anti-body that blocks blood vessel function), or PARP inhibitions combined with other drugs. Personalised approaches involving particular combinations for an individual is a possibility in the future (Keener 2021).

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6. TATTOO INK

"Tattooing involves the rapid penetration of a sterile needle into the dermis and the deposition of ink 1.5-2.0 mm below the skin's surface. The carrier solution of the ink, containing water, alcohol, and other materials, is thought to leave the dermal layer, while the pigments are trapped in the skin by fibroblasts and macrophages. Tattoo pigments have been found to leave the skin through the lymphatic system, often making their way to lymph nodes. Regulations focus on regulating tattoo ink ingredients to minimise adverse medical events and allergic reactions" (Moseman et al 2024 p5329).

Tattoo inks contain different compounds and there are regulations about concentration levels due to cancer concerns (Fox-Skelly 2025) [9]. But many inks are not compliant with the regulations.

Moseman et al (2024) analysed inks from five manufacturers used in Europe, where the "Registration, Evaluation, Authorisation, and Restriction of Chemicals" (REACH) regulations apply [10]. Nine of ten inks were not compliant with the regulations, and four contained banned ingredients. Labelling inaccuracies were common.

In terms of studies on the risk of cancer of the lymph nodes (lymphoma) (and cancers; table 6.1), Nielsen et al (2024) identified all cases of malignant lymphoma diagnosis between 2007 and 2017 among 20-60 year-olds in Sweden. This totalled 11 905 individuals, of which 1398 agreed to complete a questionnaire. These participants were age- and sex-matched to healthy controls in the Swedish population, and 4193 of them completed a questionnaire. The prevalence of a tattoo was 21% among the cancer cases and 18% among the controls. The size of the tattoo (ie: total tattooed body surface) did not influence the risk of cancer. The highest risk was diffuse large B-cell lymphoma, and follicular lymphoma.

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[9] "Tattoo inks are cocktails of organic and inorganic colour pigments, together with precursors and byproducts from the pigment synthesis, and additives. Coloured inks may contain primary aromatic amines (PAA), black inks often contain polycyclic aromatic hydrocarbons (PAH), and metals (ie: arsenic, chromium, cobalt, lead, and nickel) are found in ink of all colours. A significant and concerning number of chemicals in tattoo ink are classified as carcinogenic by the International Agency for Research on Cancer" (Nielsen et al 2024 pp1-2). Black ink, for example, contains soot products like carbon black, which are possibly carcinogenic (Clemmensen et al 2025).

[10] REACH "regulates materials that may cause irritation and gene mutation, may be carcinogens, and materials that may impact reproductive health. One important aspect of REACH regulations involves the labelling of products. Not only does a product have to display identifying information (ie: batch and lot numbers) and precautions, but a full and accurate ingredient list must be present on the packaging to be considered REACH compliant" (Moseman et al 2024 p5329).

Another study (Clemmensen et al 2025) was based on the "Danish Twin Tattoo Cohort", which was set up in 2021. There was a cohort of 2367 randomly selected twins from the Danish twin Register, and a case-control study of 316 twins born between 1960 and 1996 who volunteered to participate.

The risk of lymphoma and skin cancer were higher among tattooed than non-tattooed individuals in both parts of the study. Specifically, there were fourteen twin pairs where one twin had been tattooed and the other not.

Clemmensen et al (2025) explained: "Our study was initiated based on the suspicion that ink deposits will interact with surrounding tissue causing increased cell proliferation and thereby increase cancer risk. We term this the ink deposit conjecture. The mechanism involves an immunologic response and is recognised, for instance, in breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) – a rare type of T-cell lymphoma. We stress that this pathway does not necessarily involve specific ink agents; however, if carcinogenic compounds are present, the pathway is expectedly different but still leads to increased cancer risk" (p6).

However, causation was not established, and the authors accepted confounders; for example: "having a tattoo, especially among adolescents, has been suggested as an indicator of risky lifestyle highly associated with eg: smoking and alcohol consumption – both risk factors of certain cancer types" (Clemmensen et al 2025 p7).

STUDY	DETAILS
Barton et al (2020)	New Hampshire, USA; matched case-control design; 156 tattoo cases vs 213 controls; increased risk of early onset basal cell carcinoma
Warner et al (2020)	British Columbia, Canada; matched case-control design; 737 cases of non-Hodgkin lymphoma vs 781 controls; 373 cases of multiple myeloma vs 369 controls; no association found

(Source: Clemmensen et al 2025)

Table 6.1 - Two other studies on tattoo ink and cancer.

Overall, however, "the link between tattoos and cancer is far from cut and dried" (Fox-Skelly 2025).

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7. CO-MORBIDITIES

7.1. Long covid
7.2. Cardiovascular disease
7.3. References

7.1. LONG COVID

"Advancements in cancer treatment have contributed to improved cancer survivorship, with an estimated 18 million cancer survivors in the United States as of 2022. Given the shift from cancer representing a terminal illness to a chronic disease, it is essential to understand the health challenges faced by cancer survivors. Cancer survivors have an increased risk of stroke, cardiovascular disease, and chronic obstructive pulmonary disease. Cancer-related fatigue is also a concern, with high rates of fatigue across cancer types, resulting in limitations in daily functions. The combination of cancer treatment and the long-term health effects of survivorship results in lower self-reported quality of life" (Case et al 2026 p1).

With a weakened immune system from cancer treatment, cancer survivors are more susceptible to certain illnesses, like covid-19, and "long covid". Wang et al (2025) found that cancer survivors who had had covid-19 were more likely to develop long covid than non-cancer individuals with covid-19 infection.

Case et al (2026) explored this further with data from the 2023 "Behavioural Risk Factor Surveillance System" (BRFSS) survey in the USA. This survey randomly telephoned adults in all fifty US states, the District of Columbia, and three US territories. All variables were self-reported, including covid-19 infection (as determined by a test), cancer survivorship, and long covid (symptoms for three months or longer).

In total, 31 873 respondents reported covid-19 infection and a cancer diagnosis, of which 15.2% had long covid symptoms (compared to 13.6% in the full BRFSS sample). Long covid among cancer survivors was associated with being female, younger (18-34 years), not vaccinated (covid-19 or flu), and had diabetes, and asthma.

The characteristic of younger individuals with long covid was different to previous studies, and the researchers warned that "this trend reversal may be due to survivorship bias, as older cancer survivors who recover from covid-19 may be healthier, while those with greater health vulnerabilities may have died during acute

infection. It is important to recognise this unique pattern, as the perceived risk of severe complications from covid-19 is lower among younger age groups" (Case et al 2026 p4).

7.2. CARDIOVASCULAR DISEASE

"Cancer and cardiovascular disease (CVD) are the two leading causes of mortality in the United States, historically studied as separate clinical entities. However, emerging evidence reveals complex, bidirectional relationships between these conditions that may significantly influence patient outcomes. While cardio-oncology initially focused on cardiovascular toxicities from cancer treatments, recent research highlights that CVD itself may impact cancer progression and survival, a concept known as 'reverse cardio-oncology' [Satpathy et al 2023]" (Mehta et al 2026 p1).

Mehta et al (2026) investigated this topic using US death certificate data for 1999 to 2020. The focus was individuals who died with an underlying cause of death of cancer (nearly fourteen million adults), and the number of them who had CVD co-morbidities in the multiple causes of death section of the death certificate (32.6%).

The overall age-adjusted mortality rate (AAMR) for cancer and CVD was 47.75 per 100 000 population, but the figure was higher for males (AAMR = 62.26), Non-Hispanic Black individuals (AAMR = 57.10), and those over 65 years old (AAMR = 198.47 for 65-84 years, and 287.63 for 85 years and above). Lung cancer was "significantly higher when CVD was present", but "this association is likely attributable to profound unmeasured confounding by shared risk factors such as smoking" (Mehta et al 2026 p1).

The mechanisms behind the findings potentially included smoking (higher in males than females), healthcare access (eg: Non-Hispanic Black population and barriers to care), and chronic inflammation (Mehta et al 2026).

The researchers recommended "all caution" when interpreting the findings: "It is critical to remember that these findings are purely descriptive. Multiple causes of death do not indicate an order of occurrence and do not provide a means to determine whether CVD was a cause of death prior to either diagnosis or treatment, was a consequence of treatment or occurred independently of the cancer" (Mehta et al 2026 p5). Also the data source - death certificates - their "accuracy varies by certifier type, healthcare setting, and state

documentation standards. Direction of bias is unknown — differences could over-report or under-report true CVD burden" (Mehta et al 2026 pp5-6). The researchers continued: "When comparing death certificates to medical records and/or autopsy results, large error rates have been identified with many causes of death recorded on the certificate not being consistent with the cause of death assigned at discharge from hospital. Chronic diseases, for example, hypertension and obesity, are also often not included in the certificate data" (Mehta et al 2026 p6).

Unmeasured confounders are another potential concern, as well as lack of details about the cancers (eg: type; stage of disease; treatment), and CVD (eg: sub-types).

The findings confirmed previous studies (eg: women and breast cancer; Patnaik et al 2011).

7.3. REFERENCES

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8. MISCELLANEOUS NOVEL TREATMENTS

8.1. Bacteria and cancer
8.2. Miscellaneous

8.1. BACTERIA AND CANCER

Irit Balboul, suffering from severe pancreatic cancer in 2019, volunteered to drink a liquid containing live Salmonella typhimurium bacteria [11]. This triggered an immune response to the cancer tumour, which subsequently shrunk (Klein 2023).

"It is now clear that many bacteria are naturally attracted to tumours, which are home to a rich microbial ecosystem. This tumour microbiome can influence how cancer progresses and responds to treatment" (Klein 2023 p40).

Nejman et al (2020) were the first to find bacterial cells in an analysis of over 1500 human tumour samples, while Narunsky-Haziza et al (2022) found fungi in tumours. Specifically, Fusobacterium nucleatum bacteria have been found to promote colon cancer, and Malassezia globosa fungi to live in breast tumours (Klein 2023).

There is potential to use this knowledge to treat cancer. For example, vaccines to "train" the immune system to recognise certain microbes that live in tumours, or injecting certain bacteria that migrate to tumours and so trigger the immune system about the tumour (Klein 2023).

For example, Gniadek et al (2020) tested a single dose of attenuated Salmonella typhimurium administered orally to 22 patients with metastatic carcinoma (eg: solid tumours in the liver). This was a pilot study with individuals with life expectancy around two months. There was no survival advantage to the treatment, but there was evidence of an increase in circulating natural killer (NK) cells, which are a key aspect of the immune response.

Previous research with dogs (eg: Fritz et al 2016) using multiple doses of Salmonella had found a survival advantage in the case of metastatic osteosarcoma.

[11] Salmonella typhimurium "naturally infects and colonises solid tumours and stimulates a cellular immune response after infecting cells intra-cellularly... (Gniadek et al 2020 p217). This has been established first with mice (eg: Saltzman 2005).

References

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8.2. MISCELLANEOUS

(1) The idea of a personalised vaccine to combat cancer involves using messenger RNA (mRNA) to to trigger the immune system against the tumour cells - specifically to recognise abnormal proteins from cell mutations in cancer (Gerety 2025). "Much of cancer's biological power comes from the fact that to the body, it doesn't always seem like a pathogen. Because cancer arises from mutations in each patient's own DNA, the disease complicates our immune system's central task of differentiating between body and foreigh object, host and invader, 'self' and 'not self'" (Gerety 2025 p37).

Gerety, R.M (2025) Your personalised cancer vaccine Scientific American December, 34-41

(2) Immune checkpoint inhibitor (ICI)-based therapies "have changed the management of different cancers" (p1) with improved overall survival, progression-free survival (PFS), and objective response rate (ORR) (Porcari et al 2026).

There is growing evidence that the efficacy of ICIs in renal cell carcinoma (RCC), for example, is impacted by the composition of the gut microbiome. Where the gut

microbiota has a negative impact, faecal microbiota transplantation (FMT) is a possibility [12]. Porcari et al (2026) reported a randomised controlled trial for FMT with metastatic RCC (the TACITO trial). Forty-five patients in Italy received donor FMT (dFMT) or placebo FMT (pFMT) three times in six months while continuing with ICIs. The ORR was 52% of patients in the dFMT group compared to 32% in the pFMT group.

Put simply, the FMT enhanced the efficacy of the ICIs.

Porcari, S et al (2026) Faecal microbiota transplantation plus pembrolizumab and axitinib in metastatic renal cell carcinoma: The randomised phase 2 TACITO trial Nature Medicine (https://www.nature.com/articles/s41591-025-04189-2)

Thompson, A (2023) An intimate transplant New Scientist 18th February, 42-45

[12] FMT was first tried more generally in 1958 (Thompson 2023).