

MODIFIABLE RISK FACTORS AND CANCER IN IRELAND



National
Cancer
Registry
Ireland



ABBREVIATIONS

BCC- Basal Cell Carcinoma
BMI- Body Mass Index
EPA- Environmental Protection Agency
H. pylori- <i>Helicobacter pylori</i>
HIV- Human Immunodeficiency Virus
HPSC- Health Protection Surveillance Centre
HPV- Human Papillomavirus
HRT- Hormone Replacement Therapy
Hep-B- Hepatitis Virus B
Hep-C- Hepatitis Virus C
IARC- International Agency for Research on Cancer
KSHV- Kaposi Sarcoma Herpesvirus
NANS- National Adult Nutrition Survey
NCRI- National Cancer Registry Ireland
NMSC- Non-Melanoma Skin Cancer
PAF- Population Attributable Fraction
PCRS- Primary Care Reimbursement Service
SCC- Squamous Cell Carcinoma
SLAN- Survey on Lifestyle, Attitudes and Nutrition
UVR- Ultraviolet Radiation
WCRF- World Cancer Research Fund

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FOREWORD BY THE NCRI DIRECTOR

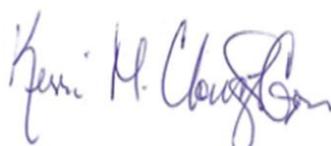
The National Cancer Registry is now in its 27th year of data collection, having begun registration of cancers and related tumours in 1994. Over this time, the registry has provided surveillance of trends in cancer incidence, treatment, survival, and prevalence, along with associated clinical and demographic aspects of the patient population. This report on the burden of cancer attributable to a selection of modifiable risk factors in Ireland will aid decisions on priorities for cancer control initiatives. This is the first time that the impact of multiple modifiable factors on cancer risk has been assessed in Ireland.

The key finding presented in this report is that in Ireland, in 2016 alone there were about 6,240 cancer cases that were attributable to the 11 modifiable risk factors chosen for this analysis. The report indicates that just among these 11 factors, 29% of cancer incidence in Ireland was potentially preventable, and notes that this is a conservative estimate. 13% of cancer incidence was attributable to smoking. Over a ten-year period ending in 2035, it is estimated that three of these factors alone, smoking, overweight and obesity and alcohol intake, will be responsible for 66,000 cancer cases.

There are some important factors to consider when interpreting these results. Due to limitations in data availability, certain modifiable risk factors, such as occupation related risks and everyday sun exposure, were not included in this report and therefore the preventable proportion of cancer incidence in Ireland is likely to be considerably higher. Where these additional risk factors were included, for example studies in the UK and US, the proportion attributable to modifiable risks were as high as 38% and 42% respectively.

The approach to this work is based on an established, high-stringency methodology and provides largely conservative estimates for the number of cancers attributable to risk factors for the whole population. It allows for international comparisons and will provide evidence to inform debate on cancer prevention in Ireland. The stringency of the methods employed means that, in some cases, the figures arrived at may also be lower than other equivalent analyses. This work is intended to be interpreted at a population level and is not designed to provide an assessment of cancer risk in an individual which is highly complex and relating to many factors, such as length of exposure to the risk factors, interactions of different behaviours, as well as demographic characteristics, individual genetics and other protective behaviours, as well as chance. Individuals who are concerned about their cancer risk should seek the advice of a medical professional.

This report builds on the previous NCRI investigation into projections of cancer incidence and reinforces the important role that cancer prevention strategies will have in ensuring that projected increases in cancer incidence are not realised. It is recommended that the findings in this report are used for future health related policy planning.



Director, National Cancer Registry



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REPORT AT A GLANCE

Who are we, and what do we do?

The National Cancer Registry of Ireland (NCRI) works on behalf of the Department of Health and collects information from all hospitals in Ireland on the number of persons diagnosed with cancer and the types of cancer they have.

NCRI also follows up the numbers dying from their cancer or from other causes. This allows the monitoring of trends and outcomes in different cancer types, which in turn assists with the planning and management of services. All the patient's personal and private details are removed before summaries of this information are made available to the public and health professionals through our annual cancer report and other reports on our website.

How are the numbers calculated?

NCRI data on the number of cancer cases in 2016 was utilised for this report. Data were also collected from a variety of sources to determine both the extent to which the Irish population are exposed to each risk factor and the likelihood of being diagnosed from cancer as a result of the exposure.

A modifiable risk factor is a behaviour or exposure that can potentially be changed, resulting in a change in risk of disease. In relation to cancer, these include smoking, infection, being overweight or obese, alcohol intake, sunburn, sunbed history, radiation, processed meat intake, hormonal replacement therapy, oral contraceptive, lack of physical activity, and exposure to fine particulate air pollution.

All of this information was inputted to formulae to calculate the percentages and numbers of cancer cases attributable to each risk factor.

In addition, the number of cancer cases associated with smoking, overweight and obesity, and alcohol intake that would occur in 2035 were estimated depending on whether current estimated attributable risks remained the same or if there were changes in exposure to the risk factors.

What have we found?

In 2016, 3/10 of all invasive cancers (i.e. excluding non-melanoma skin cancer (NMSC)) were attributable specifically to the sum of the 11 modifiable risk factors examined. This suggests that at least 6,240 cancer cases were potentially preventable in Ireland in 2016, and the true figure is likely to be higher. With 2,780 diagnoses or about 1/8 of all invasive cancer cases, smoking (including passive smoking) was associated with the highest attributable burden. By 2035, assuming these risk estimates continue to apply, it is estimated that 4,660 cases of invasive cancer per year will be attributable to smoking, 1,790 cancer cases will be attributable to overweight and obesity, and 850 cancer cases will be attributable to alcohol intake. It is essential that measures are undertaken and continued, especially at a population level, to ensure that possible increases in cancer cases in the future do not become a reality. It is recommended that the findings in this report are used for future health-related policy planning.

TECHNICAL SUMMARY

The proportion of primary cancer incidence attributable to modifiable risk factors in Ireland.

Cancer cases attributable to modifiable risk factors, 2016.

- The population attributable fractions (PAFs) are interpreted as the proportion of cases that would be prevented if exposure to a causal factor in the entire population was adjusted to the level of the reference category (i.e. ideal exposure).
- Cancer type and risk factor combinations were included using stringent definitions by the International Agency for Research on Cancer (IARC) or World Cancer Research Fund (WCRF) that there was “sufficient” (IARC) or “convincing” (WCRF) evidence of a **causal** association with a specific cancer type. It is important to consider that these classifications describe the level of scientific evidence that a risk factor is linked to a cancer, but not how much cancer they cause.
- This report estimates that in 2016, 29.3% of all cancer cases (excluding non-melanoma skin cancer (NMSC)) were attributable to the 11 modifiable specific risk factors examined (see list in *Table 1*).
- 6,238 cancer cases (out of a total of 21,315) were potentially preventable in Ireland in 2016.
- This is a conservative estimate for a number of reasons. For example, risks associated with occupation were not accounted for here and may be examined in a further analysis. In the UK, 3.8% of cancer cases were attributable to occupation. Due to a lack of data on sun exposure behaviours among the population in Ireland, everyday exposure to ultra-violet radiation (UVR) was not included either; only whether a person had ever been sunburned or used a sunbed (where Irish data is available).
- Smoking, overweight and obesity, and infections were the top three risk factors in Ireland:
 - Smoking (including passive smoking in the home) was the risk factor with the highest attributable cases of all cancer (excluding NMSC) at 13%, accounting for 2,779 cases.
 - 5% of cancer cases (excluding NMSC) were attributable to being overweight or obese, equating to 1,061 cancer cases in Ireland in 2016.
 - A number of carcinogenic infection types (HPV, *H. pylori*, EBV, Hep B, Hep C and HIV) were grouped together; 3.6% of cancer (excluding NMSC) incidence was attributable to these infections.

• PAFs and attributable cases of cancer by risk factor are summarised in *Table 1*.

• Lung cancer had the highest number of cases attributable to modifiable risk factors in both males and females, followed by colon cancer in males and breast cancer in females.

• PAFs and attributable cancer cases by cancer type in males and females are presented in *Tables 2 and 3* respectively.

Projections of cancer cases attributable to modifiable risk factors to 2035.

• Cancer cases (excluding NMSC) attributable to smoking (excluding passive smoking), overweight and obesity, and alcohol intake were modelled to 2035 on the assumption that current PAFs remain the same (i.e. that only population numbers and age-structure change):

- In 2035, it is estimated that:
 - 4,662 cancer cases will be attributable to smoking.

- 1,788 cancer cases will be attributable to overweight and obesity.
- 851 cancer cases will be attributable to alcohol intake.
- Over a 10-year period ending in 2035, it is estimated that a cumulative total of 66,343 cancer cases will be

attributable to smoking, overweight and obesity and alcohol intake.

- In addition, projections were calculated assuming a variety of different scenarios related to changes in the prevalence of risk factors — for example, if the prevalence of current smokers were reduced from 29% to 5%. See pages 33-37 for further details.

Table 1. Population attributable fractions (PAFs) and attributable cases of all cancer excluding NMSC by risk factor in Ireland, 2016.

Risk Factor	PAF (%)	Attributable cases of all cancer excluding NMSC
Smoking	13.0	2779
Overweight and obesity	5.0	1061
Infection	3.6	766
Alcohol intake	2.4	506
Single episode of sunburn and sunbed use	1.9	414
Radiation	1.1	237
Processed meat intake	0.8	173
Oral contraceptive*	0.5	114
Use of hormonal replacement therapy*	0.5	114
Lack of physical activity	0.2	38
Fine particulate air pollution	0.2	36

*Please note, although oral contraceptive and hormonal replacement therapy usage can increase the risk of certain cancers, they can also decrease the risk of other cancer types. Therefore, it is likely that the net effect of cancer cases attributable to oral contraceptive and hormonal replacement therapy use is lower than presented here.

Table 2. Male population attributable fractions (PAFs) and attributable cases by cancer type in Ireland, 2016.

Cancer type	PAF (%)	Attributable cases
Lung	81.2	996
Colon	37.6	346
Rectum	38.7	213
Melanoma	38.3	193
Stomach	54.0	192
Oesophagus	59.3	171
Bladder	49.7	154
Kidney	30.6	132
Larynx	74.4	105
Liver	53.2	96
Oral Cavity	50.2	86
Pancreas	34.9	82
Pharynx	67.4	80
Leukaemia	11.6	38
Hodgkin Lymphoma	40.7	36
Myeloma	11.6	24
Penis	63.3	23
Non-Hodgkin Lymphoma	3.2	21
Anus	88.7	19
Nasopharynx	85.3	12
Kaposi Sarcoma	100.0	8
Thyroid	11.8	8
Brain & CNS	1.8	4
Gallbladder	11.5	3
Bone	2.6	1
Conjunctiva	0.7	0

Table 3. Female population attributable fractions (PAFs) and attributable cases by cancer type in Ireland, 2016.

Cancer	PAF%	Attributable cases
Lung	80.6	880
Breast	20.7	650
Cervix	93.7	266
Melanoma	37.6	221
Colon	25.0	197
Uterus	33.9	179
Stomach	52.5	94
Kidney	35.6	90
Oesophagus	56.9	79
Pancreas	31.2	72
Rectum	25.3	65
Bladder	48.1	54
Liver	48.1	42
Vulva	68.8	38
Anus	92.5	32
Oral Cavity	34.5	30
Leukaemia	14.0	28
Ovary	8.2	28
Hodgkin Lymphoma	40.7	25
Non-Hodgkin Lymphoma	4.8	23
Thyroid	11.7	20
Pharynx	53.5	19
Larynx	68.6	16
Myeloma	7.3	11
Gallbladder	21.1	9
Vagina	75.0	7
Nasopharynx	84.8	5
Meningioma	13.5	3
Brain & CNS	1.8	2
Kaposi Sarcoma	100.0	1
Bone	2.6	1

METHODOLOGY

- Modifiable risk factors were selected for this investigation if classified by the International Agency for Research on Cancer (IARC) or World Cancer Research Fund (WCRF) as having “sufficient” (IARC) or “convincing” (WCRF) evidence of a causal association.
- The PAF is interpreted as the proportion of cases that would be prevented if exposure to a causal factor in the entire population was adjusted to the level of the reference category (i.e. the level of ideal exposure to a risk factor, usually zero).
- Calculating PAF as percentages and attributable cases requires information on the **population prevalence** of each risk factor, the **relative risk** associated with each risk factor, and the **incidence** of each cancer type in the population.
- Cancer incidence data for 2016 was obtained for the Irish population from the NCRI which records all incident cancers in Ireland. All age groups were included in the analysis. Results were calculated for males, females and all persons. For each potential risk factor, literature was reviewed to identify the most suitable Irish-based population prevalence data, preferably nationally representative surveys.
- When calculating PAFs, the amount of time between exposure to the risk factor and cancer outcome (time lag) was considered. This can be difficult to determine as the amount of time varies depending on the risk factor and the cancer site. However, based on methodology used by similar national studies in other jurisdictions, a 10-year lag was applied. When exposure of the Irish population to risk factors was not available for 2006, data from the nearest timeframe was employed in the analyses. See methodology annex for further details.
- The UK’s recently systematically searched and published relative risks were obtained. More recent published literature was then reviewed to determine if there were any more recent meta-analyses available.
- It is important to note the difference between attributable risk and relative risk, which are mentioned throughout the report. Relative risk refers to magnitude of an association between exposure and disease, based on the incidence of disease in the exposed group relative to the unexposed group. Attributable risk refers to the absolute difference in incidence between an exposed and unexposed group. In some instances, a high relative risk may translate to a small attributable risk.
- The formulae with which the PAFs are calculated are given in the methodology annex.
- PAFs for all risk factors combined, for each cancer type, were obtained by first applying the first relevant PAF in the sequence to the total number of observed cases, to obtain the number of cases attributable to that factor only. Resultant figures were then summed across all relevant cancers for a given risk factor.
- Each subsequent PAF in the sequence was applied only to the number of observed cases not yet explained by the risk factors earlier in the sequence. This approach ensures that the overall number of attributable cases is not over-estimated, but has a significant bearing on the measurement of the number of cases attributed to each risk factor and cancer type as a number of cases are removed from the calculation for each analysis. This results in the calculation of a lower number of preventable cases for those PAFs applied later in the sequence, i.e. PAFs of a lower value. However, use of a different sequence does not change the overall result in terms of the total number or proportion of cancer cases attributable to the risk factors in combination.

- Models were developed to project all cancer cases (excluding NMSC) to 2035 that are attributable to the following major risk factors; smoking (excluding passive smoking), overweight and obesity, and alcohol intake. In order to calculate the cancer cases attributable to each risk factor, we applied the PAF calculated and reported for 2006 exposure for males and females to projected incidence. Projected

incidence assumed that recent age-specific incidence rates applied to future populations.

- Various target and trend scenarios were also applied to these projection models.
- Further details on the methodology are presented in the methodology annex.

RISK FACTOR 1. SMOKING

- Smoking is the biggest cause of cancer across the world and causes 15 different types of cancers (see *Figure 1.1*) (1).

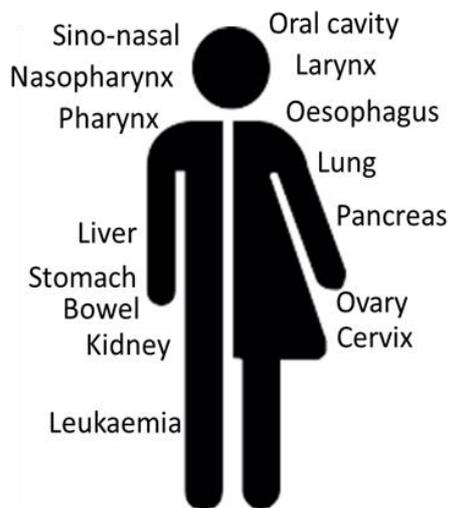


Fig 1.1 Smoking is a risk factor for each of these cancer types.

- Cigarettes contain thousands of compounds, including over 60 carcinogens, which enter our bloodstream and can affect the entire body (2).
- Current smoking, being an ex-smoker and exposure to smoking in the home was included in this analysis, see methodology annex for further details.
- The 2007 SLAN survey reported that in Ireland, 48% of people had smoked at some point in their lives, with 29% reporting being current smokers (3).
- Passive smoking (the involuntary inhaling of smoke from other people's cigarettes) is also a risk factor for lung cancer and was therefore considered in this analysis. 59% of people reported smoking was not allowed anywhere in their home (3), although figures on passive smoking outside the home were not available.

- There are different levels of risk associated with being a current or former smoker, or being exposed to second-hand smoke and the risk also varies depending on the cancer site. The lungs are the most at risk of developing cancer with a current smoker being 9 times more likely to develop lung cancer compared to someone who has never smoked (4).
- This risk is reduced for former smokers to less than 4 times that of never smokers (4). Stopping smoking completely is recommended.
- Using our conservative analyses, at least 76% of lung cancers in Ireland are attributable to smoking (including passive smoking in the home), with the larynx and bladder being the cancer sites with the next highest percentages attributable to smoking (*Figure 1.2*).

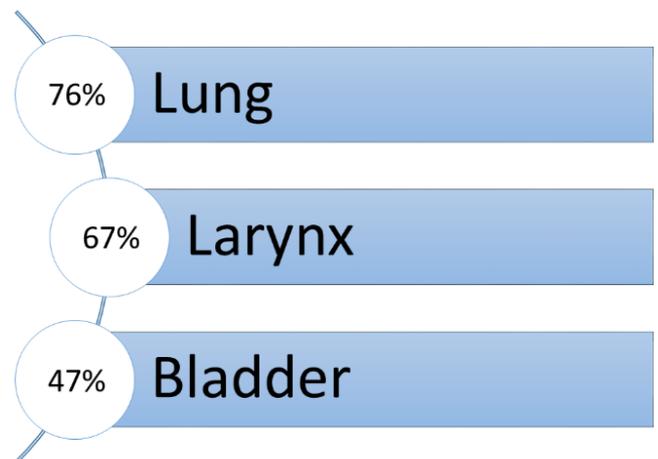
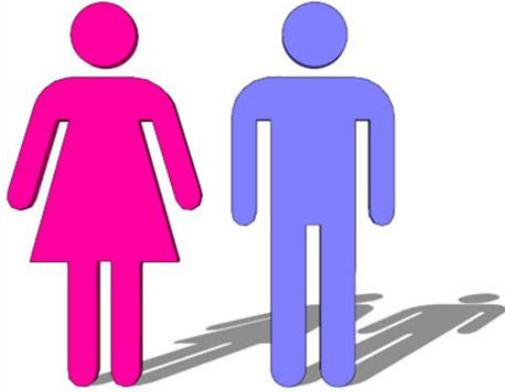


Fig 1.2. Top 3 cancer sites associated with smoking and the PAF%

- Overall, smoking (including passive smoking) is the biggest contributor to cancer in Ireland and is **responsible for 13% of all cancer** (excluding NMSC). The estimated total of cancer cases attributable to smoking in Ireland in 2016 was **2,779**, and a similar figure is likely to apply currently. *Figure 1.3* presents the difference between male and female cancer incidence related to smoking.

PAF: 11.4%.
Attributable
cases: 1,150.



PAF: 14.5%.
Attributable
cases: 1,629.

Fig 1.3. PAF% and attributable cases, males and females.

- These estimates are likely to be conservative as although they account for passive smoking in the home, they do not account for other regular passive smoke exposures (i.e. outside the home), such as in vehicles and public spaces. Additionally, smoking may interact with other risk factors to further increase cancer risk. For example, in lung cancer there exists a synergistic interaction between radon exposure and smoking which is not accounted for here.
- Projections of avoidable incidence of cancer as a result of tobacco smoking are discussed in projections section (page 33).

How do these figures compare?

The PAFs for smoking and cancer incidence in Ireland are similar to those reported in Australia and the UK at 13.4% and 15.1% respectively (5, 6).

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RISK FACTOR 2. OVERWEIGHT AND OBESITY

- According to IARC, having a body mass index (BMI) of 25 kg/m³ or more — defined as being overweight (25-29.9 kg/m³) or obese (≥30 kg/m³) — is a risk factor for developing certain forms of cancer (1).
- Keeping a moderate weight reduces the risk of 13 different types of cancer; those associated with being overweight or obese are shown in *Figure 2.1*.

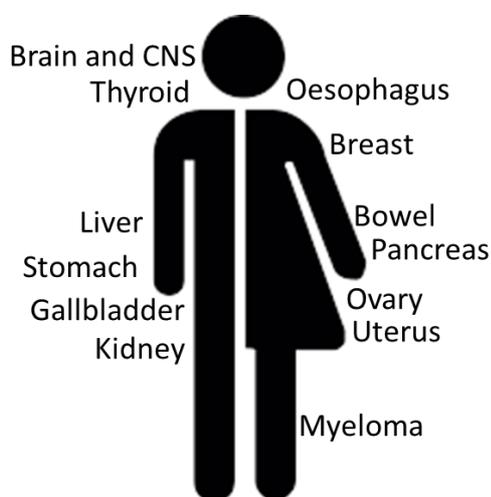


Fig 2.1. Being overweight or obese is a risk factor for each of these cancer types.

- There are a number of ways in which being overweight or obese is thought to contribute to risk of developing of cancer; the major mechanisms include changes in sex hormone metabolism, increased insulin levels and adipokine pathophysiology, as well as systemic inflammatory changes (2).
- Data on the rates of overweight and obesity in Ireland was reported in 2007 SLAN report and used in this analysis. This report found that, of samples of respondents that were independently measured, 30% of men and 40% of women had BMIs within the healthy range (3). 45% of men and 33% of women were reported to be overweight, while 24% of men and 26% of women were reported to be obese.

- In 2019, the latest data from the national longitudinal study “Growing Up in Ireland” showed that 15% of five-year olds were overweight and 5% were obese (5). This suggests that overweight and obesity may remain a health challenge in Ireland in the future.
- The level of risk associated with BMI is different depending on whether the person is overweight or obese and which cancer type is involved. The cancer sites associated with the highest relative risk as a result of being overweight or obese are the oesophagus (adenocarcinoma type only) and the uterus. It should be noted that although these cancers have the highest relative risk, due to lower incidence they do not contribute as impactfully to numbers at the population level.
- In Ireland, overweight and obesity contributes the highest proportion of attributable cases for cancer in the kidney, liver and gallbladder (*Figure 2.2*). Of these, cancer of the kidney had the highest number of cases (155) attributable to a high BMI in 2016. However, this was exceeded by cancer of the colon that were attributable to overweight and obesity at 182 cases (lower PAF, 11% but a more common cancer).

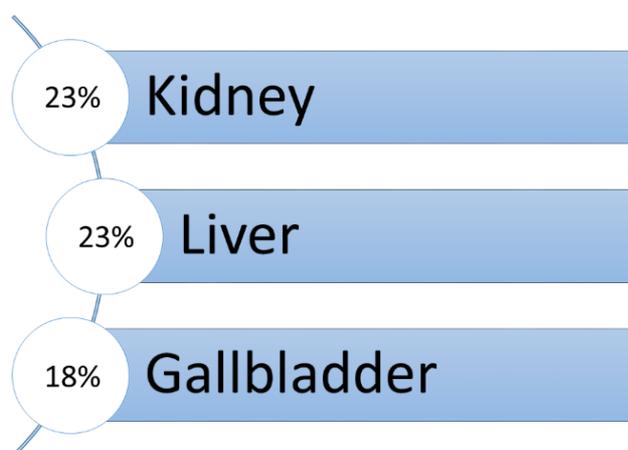


Fig 2.2. Top 3 cancer sites associated with being overweight or obese and the PAF%

- Overall, **5.0% of all cancer cases** (excluding NMSC) were attributable to a high BMI in Ireland in 2016. In total, an estimated **1,061** cancer cases were attributable to being overweight or obese in Ireland in 2016, and a similar number is likely to currently apply. See *Figure 2.3* for comparisons between male and female cases.

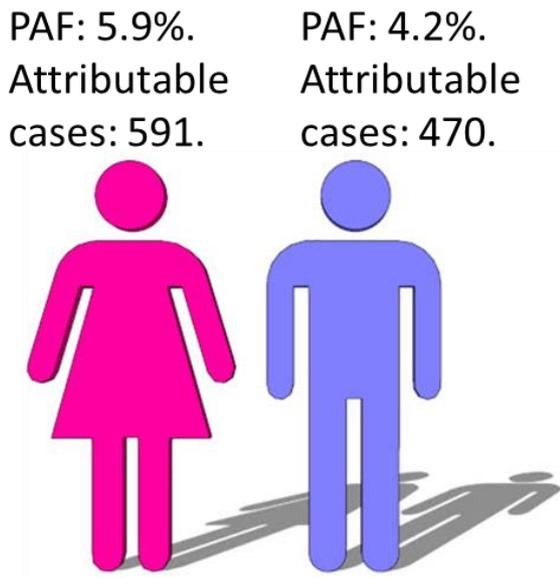


Fig 2.3. PAF% and attributable cases, males and females.

- Projections of cancer cases (all cancer excluding NMSC) to 2035 attributable to a high BMI are reported in the projections section (page 33).

How do these figures compare?

The PAFs for overweight and obesity and cancer incidence in Ireland are similar to those reported previously in Ireland (4.5%), as well as in France and the UK at 5.4% and 6.3% respectively (6, 7, 8).

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RISK FACTOR 3. INFECTIONS

- According to IARC, infection with specific types of bacteria and viruses is defined as a risk factor for developing cancer (1).
- These biological agents include hepatitis virus B (Hep-B) and C (Hep-C), Epstein-Barr virus (EBV), human immunodeficiency virus (HIV), human papillomavirus (HPV), Kaposi Sarcoma Herpesvirus (KSHV) and *Helicobacter pylori* (*H. pylori*).
- The 14 cancer types that these biological agents are associated with are shown in *Figure 3.1*.

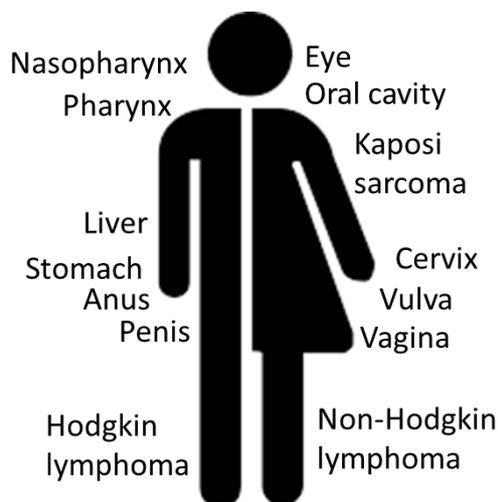


Fig 3.1. Infections are a risk factor for each of these cancer types.

- The ways in which these bacteria and viruses act as carcinogens have yet to be fully determined, and vary depending on the type. However, it is known that they can disrupt signalling that normally regulates cell growth and proliferation. They can also weaken the immune system and cause chronic inflammation, which can lead to cancer (1).
- The Health Protection Surveillance Centre (HPSC) reports on the prevalence of many infection types in the Irish population. However, due to the absence of Irish information, data from Northern Ireland needed to be used in the case of *H. pylori*, and

pre-calculated PAFs were used to calculate incidence attributable to EBV, HPV and KSHV. See methodology annex for further details.

- There is a wide range in the level of risk associated with each infection and cancer type combination; for example, Hep-C is associated with a risk of non-Hodgkin lymphoma 2 times higher and a risk of liver cancer almost 24 times higher in those exposed compared to non-exposed. Further information on risk factors related to infection is presented in the methodology annex.
- In Ireland, HPV, *H. pylori* and EBV are the top 3 infection types in terms of the percentage of all cancers (excluding NMSC) attributable to specific infectious agents (*Figure 3.2*). 397 cancers (exc NMSC) were attributable to HPV alone in 2016.

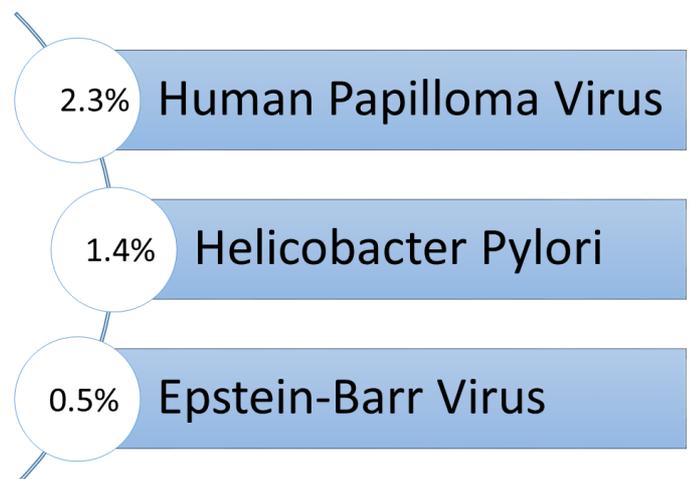


Fig 3.2. Top 3 infection types associated with cancer and the PAF% (all cancer exc NMSC)

- In terms of infection and specific cancer types, 257 cervical cancers were attributable to HPV while 208 stomach cancer (non-cardia) cases were attributable to *H. pylori* in 2016. See *Figure 3.3* for the PAF for each infection type and cancer site combination.

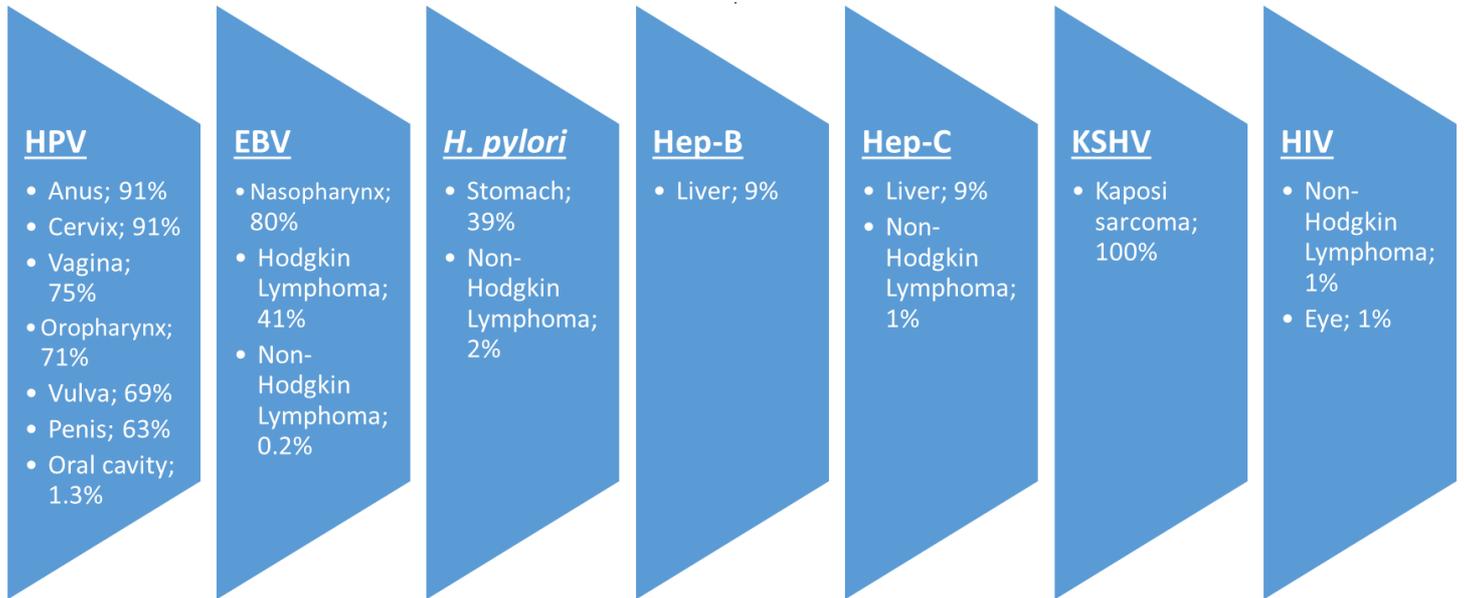


Fig 2.3. PAF% for each infection and cancer site combination

- Overall, these infections are **responsible for 3.6% of all cancer** (excluding NMSC). The estimated total of cancer cases attributable to infections in Ireland in 2016 was **766**. See Figure 3.4 for comparisons of male and female cases.

PAF: 4.8%.
Attributable cases: 483.

PAF: 2.5%.
Attributable cases: 283.

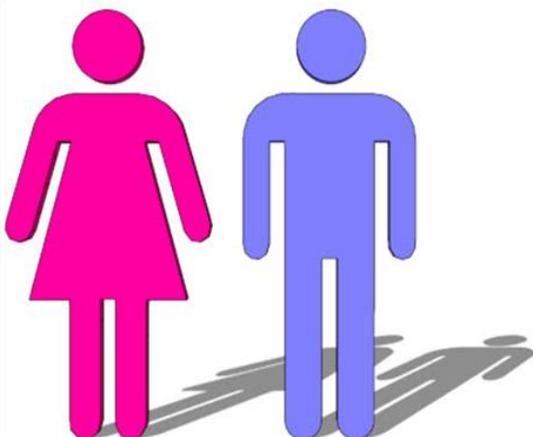


Fig 3.4. PAF% and attributable cases, males and females.

How do these figures compare?

The PAFs for infection and cancer incidence are similar to, but slightly higher than, those reported in France and the UK, at 4.0% and 3.6% respectively (2, 3).

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RISK FACTOR 4. ALCOHOL INTAKE

- Both IARC and WCRF state there is sufficient or convincing evidence of a causal association between alcohol intake and developing some specific forms of cancer (1, 2).
- Limiting alcohol intake reduces the risk of 7 different types of cancer; those associated with alcohol intake are shown in *Figure 4.1*.

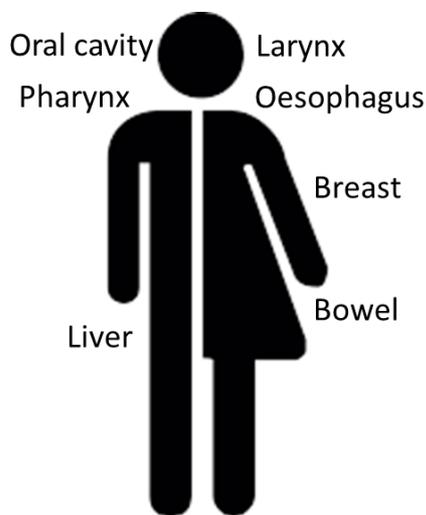


Fig 4.1. Alcohol consumption is a risk factor for each of these cancer types.

- The mechanisms through which alcohol intake increases cancer risk are not yet well defined but likely to include genotoxic effects, increased oestrogen, cellular stress, changes in folate metabolism and inflammation (3).
- National Adult Nutrition Survey (NANS) data on alcohol intake was categorised into 4 groups: no alcohol, light, moderate, or heavy intake (see methodology). 86% of the adult population were alcohol consumers. 45% of men and 23% of women were moderate alcohol consumers, while 5% of men and 0.5% of women were heavy alcohol consumers (4).
- The NANS report highlighted that the Department of Health has recommended that men consume no

more than 17 Irish 'standard drinks' and women no more than 11 per week. Among Irish alcohol consumers aged 18-64 years, 29% of men and 24% of women report consuming higher than the maximum recommend weekly alcohol intake (4).

- The level of risk associated with alcohol intake and cancer types is different depending on the amount of alcohol consumed and which cancer type is involved. For example, compared with a non-alcohol consumer, a person with light alcohol intake has a 1.3 fold increased risk of a specific type of oesophageal cancer (squamous cell carcinoma [SCC]), and moderate and heavy consumers are 2.6 and 5.5 times more likely to develop oesophageal SCC, respectively. A heavy alcohol consumer is also 5 times more likely to develop pharyngeal and oral cavity cancer. See methodology for further breakdown.
- In Ireland, of the cancers defined as alcohol-related in this report, those with the highest proportion attributable to alcohol intake were cancers in the pharynx, oral cavity, and larynx (*Figure 4.2*). A smaller proportion (7.5%) of female breast cancer is attributable to alcohol intake but this translates to a large number (223) of cases.

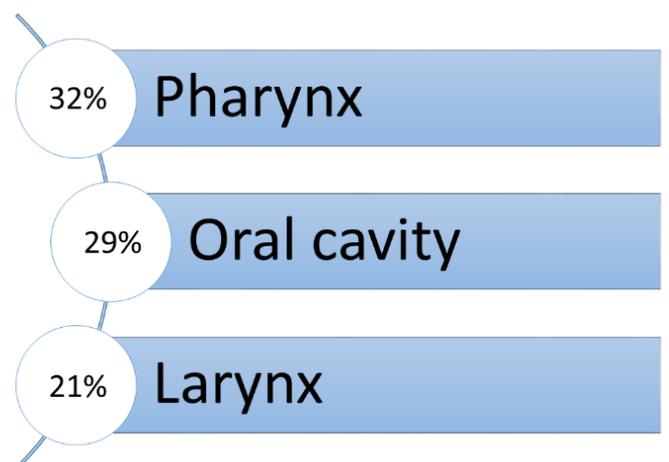


Fig 4.2. Top 3 cancer sites associated with alcohol consumption and the PAF%

- Overall, **2.4% of all cancer** (excluding NMSC) was attributable to alcohol intake (as a single factor) in Ireland in 2016. The estimated total of cancer cases attributable to drinking alcohol in Ireland in 2016 was **506**, and a similar figure is likely to apply currently. See *Figure 4.3* for differences between male and female incidence.

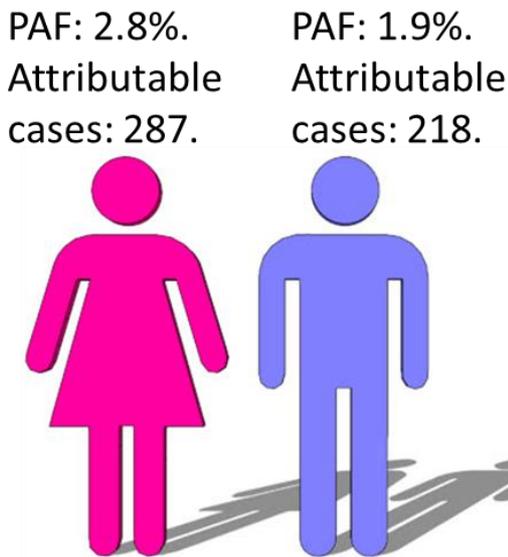


Fig 4.3. PAF% and attributable cases, males and females.

- In 2013, Laffoy et al. published estimates of cancer incidence due to alcohol intake in Ireland and estimated higher PAFs; 4.7% in males and 4.2% in females (7). The differences between the PAFs reported here and previous Irish estimates are explained by methodological differences. For example, Laffoy et al. used SLAN data, adjusted for self-reporting, and estimates of relative risks based on earlier studies. In this analysis, NANS data and updated relative risks based on a 2015 meta-analysis were applied. Differences in the cancer site inclusion criteria between the two studies also contribute, but to a lesser extent, to differences.
- Alcohol may interact with other risk factors to further increase cancer risk, for example there exists a synergistic interaction between alcohol intake with infections and smoking which is not accounted for here (1).

How do these figures compare?

The PAFs for alcohol intake and cancer incidence in Ireland are similar to those reported by Australia and the UK, 2.8% and 3.3% respectively (5,6). They are lower than figures previously reported in Ireland as 4.7% in males and 4.2% in females, due to methodological differences (see text) (7).

References

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RISK FACTOR 5. SINGLE EPISODE OF SUNBURN & SUNBED USE

- IARC state there is sufficient evidence of a causal association between exposure to solar radiation, as well as ultraviolet radiation-emitting tanning devices, and developing melanoma skin cancer (1).
- This report focuses on the fraction of cancer attributable to sunburn history (at least single episode) and sunbed usage. It does not include the fraction attributable to everyday sun exposure due to lack of fuller data on Irish sun-exposure behaviours. Given the high prevalence of cancers associated with excess sun exposure in Ireland, there is a need for further analysis to be undertaken to establish a complete picture of the impact of sun exposure.
- Excessive exposure to solar radiation can induce DNA damage in the skin. Over time, skin cancer may develop due to a build-up of this damage that causes the cells to start growing out of control (1).
- There is limited data available on sun-exposure behaviours of the Irish population. Routine monitoring of sun exposure is important and would help determine the risk of cancer attributable to everyday sun exposure.
- Surveys from Northern Ireland reported that 40% of people were never sunburned, and this figure has been used in this report. There is a 92% increase risk of melanoma of the skin associated with ever having been sunburned. See methodology annex for details.

Table 5. Population attributable fractions (PAF) and attributable cases; single episode of sunburn, sunbed usage, skin cancer type.

Skin cancer type	Male		Female		Persons	
	PAF%	Attributable cases	PAF%	Attributable cases	PAF%	Attributable cases
<u>SCC</u>						
Sunburn	15.5	295	15	154	15.3	448
Sunbed	11.3	182	11.3	98	11.3	280
<u>BCC</u>						
Sunburn	26.8	1034	26.1	837	26.5	1871
Sunbed	5.2	148	5.2	123	5.2	271
<u>Melanoma</u>						
Sunburn	35.9	181	35.2	207	35.5	388
Sunbed	3.7	12	3.7	14	3.7	26

- The Irish Cancer Society conduct surveys on sunbed usage in Ireland. Results from 2007 found that 19% of people had used a sunbed at least once. There is a 20% increased risk of melanoma associated with ever having used a sunbed.
- Due to the influence of sunburn (single episode and sunbed exposures) on non-melanoma skin cancer, we have also reported the attributable fractions on both basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) in this section (see methodology annex for risk increases). However, it is important to note that these numbers are not included in the overall PAF analyses presented elsewhere in this report (i.e. for the “all cancer” group). Note also that pre-cancerous (“in situ”) skin lesions are excluded for both melanoma and non-melanoma morphologies.
- See *Table 5* for PAFs and cases attributable to sunburn (single episode) and sunbed usage for BCC, SCC and melanoma.
- Overall, **1.9% of all cancer (excluding NMSC)**, i.e. the summary statistic presented for other risk factors in this report, were attributable to having a single episode of sunburn or use of sunbeds in Ireland in 2016. This figure relates to melanomas only. The estimated total of melanoma cases attributable to sunburn (ever sunburned) and sunbed exposure in Ireland in 2016 was **414**. See *Figure 5.1* for differences between male and female incidence.
- It is worth considering that the UK reported that **3.8% of all cancer and 86.5% of melanoma** was attributable to UV exposure, which is likely a more accurate reflection of the burden of cancer resulting from UV exposure. Applying this PAF to our data would result in a doubling of cancer incidence relating to UV exposure. The UK estimated the UV-

attributable cases occurring in 2010 as the difference between the number observed and those that would have been expected with a theoretical-minimum-risk exposure distribution, based on historical data from UK (estimated incidence rates for the generation of individuals born in 1903, resident in the South Thames region of England).

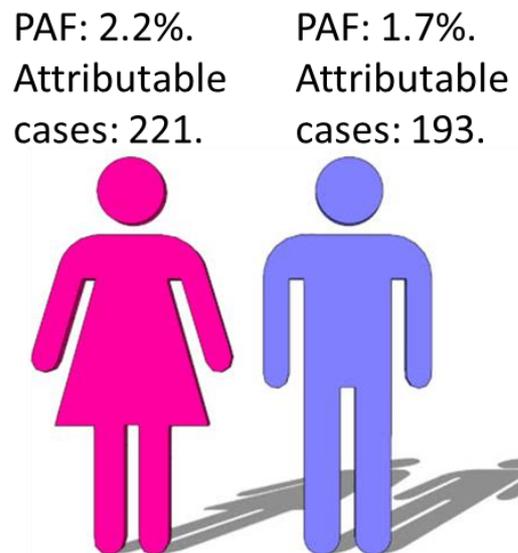


Fig 5.1. PAF% and attributable cases, males and females.

References

1. IARC Working Group on the Evaluation of Carcinogenic Risk to Humans. Radiation. Lyon (FR): International Agency for Research on Cancer; 2012. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 100D.) Solar and Ultraviolet Radiation. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK304366/>

RISK FACTOR 6. IONIZING RADIATION

- This section describes the risk of cancer associated with exposure to ionizing radiations (including radon, diagnostic radiation and background radiation). These are defined by IARC as having sufficient evidence of carcinogenicity in humans and while such radiation is not necessarily a modifiable risk factor it is generally considered a source of preventable cancer cases (1).

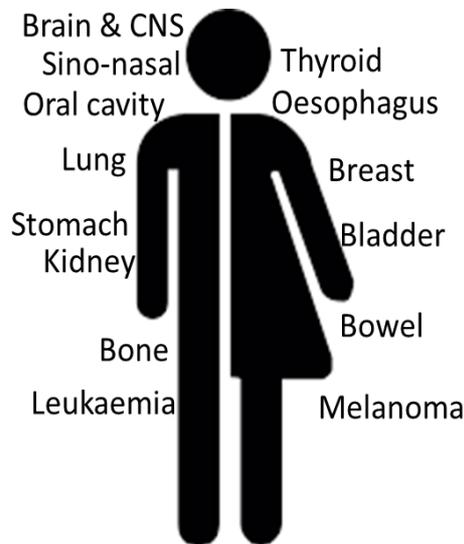
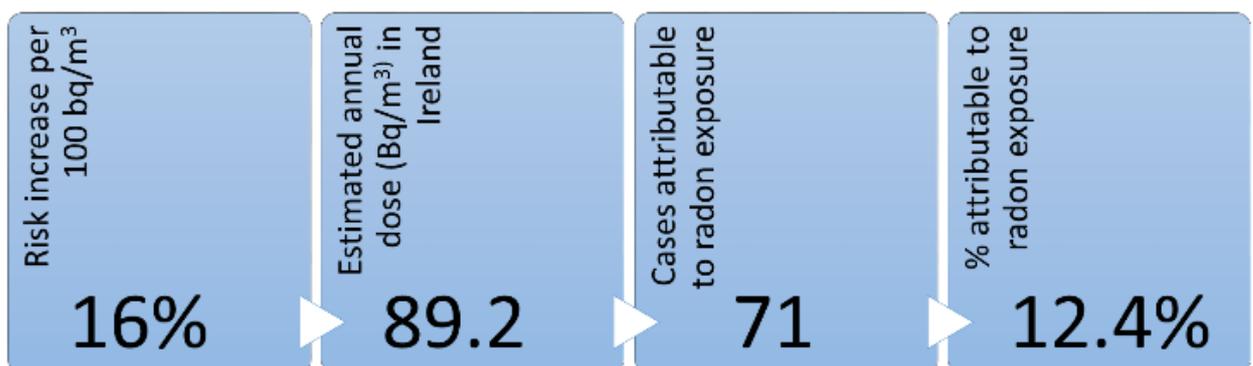


Fig 6.1. Radiation is a risk factor for each of these cancer types.

- These types of radiation are associated with an increased risk of 13 different types of cancer, as shown in *Figure 6.1*.
- Radon is a natural radioactive gas that is produced as uranium and thorium (of which small amounts are found in soil and rock) decay. Radon is thought to be carcinogenic to the lung as a result of its production of reactive oxygen species which cause DNA damage.
- Radon may be present in the home as a result of building construction practices. The National Radon Survey reported the mean indoor radon concentration as 89 Bq/m³ and that approximately a third of Ireland was classified as a high-radon area between 1992 and 1997 (2). See *Figure 6.2* for risk of lung cancer associated with radon in Ireland (the % attributable risk shown is after smoking has been accounted for).
- Background radiation includes cosmic radiation, gamma radiation from soils and radioactivity in food radiation and is associated with small increases in risks of many different cancer types (see methodology annex). Diagnostic radiation includes X-rays and radioactive tracers.

Fig 6.2 Radon and lung cancer



- Cancer of the bladder is most significantly associated with diagnostic radiation, with 1.9% of cases being attributable. Leukaemia is most highly associated with background radiation, with 15.1% of leukaemia excluding chronic lymphocytic leukaemia and 9% of all leukaemia cases being attributable.
- Overall, **1.1% of all cancer (excluding NMSC)** was attributable to radiation in Ireland in 2016. The estimated total number of cancer cases attributable to ionizing radiation was **237**. See *Figure 6.3* for male and female comparisons.

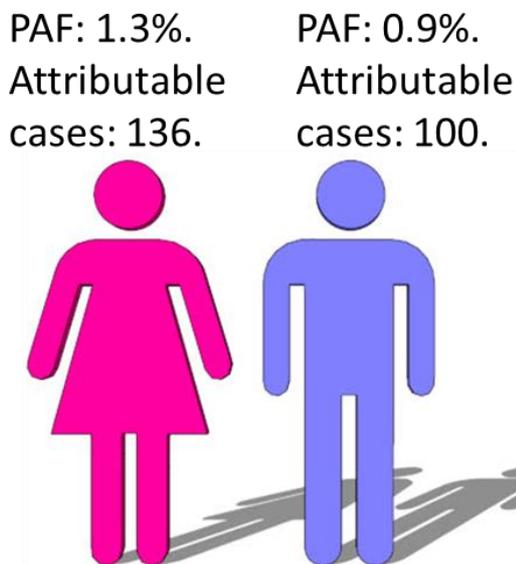


Fig 6.3. PAF% and attributable cases, males and females.

How do these figures compare?

The figures reported here are similar to those from the international literature. The UK reported a PAF of 1.9% for radiation, while France report PAFs of 1.2% and 0.7% for radon and diagnostic radiation respectively (3, 4).

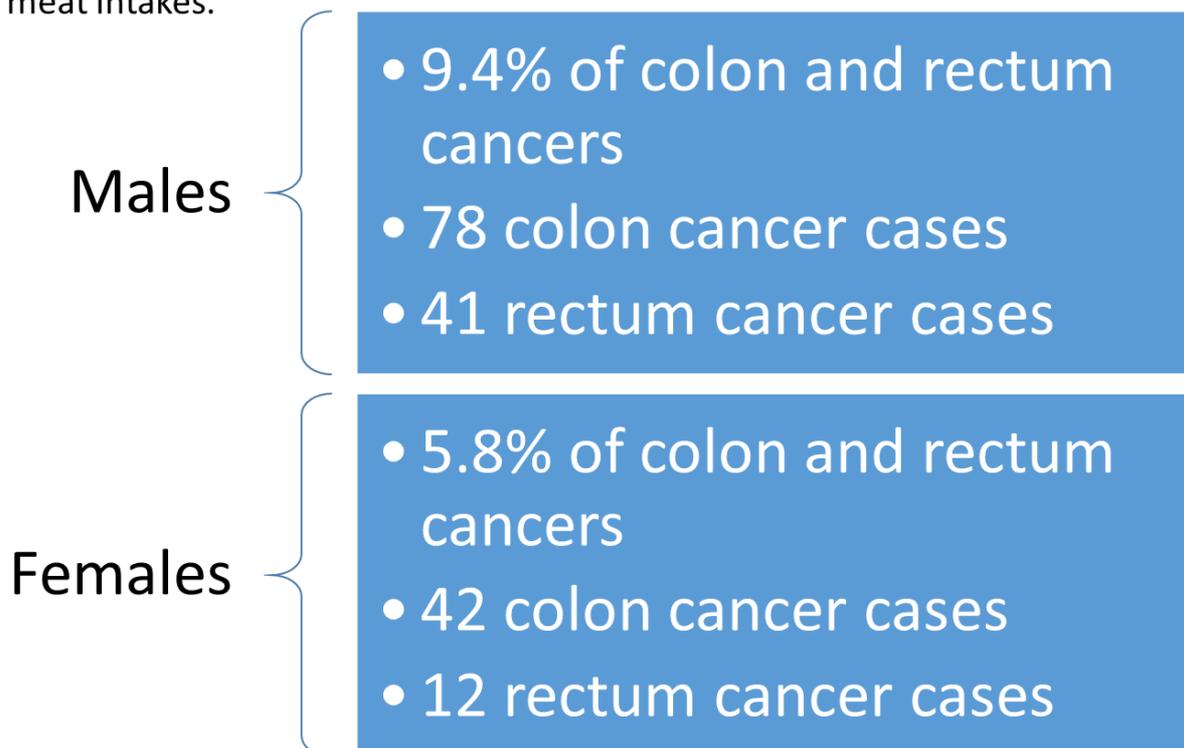
References

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RISK FACTOR 7. PROCESSED MEAT INTAKE

- The WCRF and IARC state that high processed meat intake is associated with colorectal cancer and recommend that people eat little, if any, processed meat (1, 2).
- Processed meat is defined by WCRF as meat that has been “transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation”. Processed meat can include ham, salami, bacon and some sausages such as frankfurters and chorizo. Minced meats such as fresh sausages may sometimes, though not always, count as processed meat (1).
- Many of the preservation methods used to create processed meat are known to generate carcinogens (1).
- According to NANS data, men and women in Ireland consume an average of 42.7 g and 23.9 g of processed meat per day respectively (3).
- A recent review by WCRF concluded that, for adults in Europe, there is a 13% increased risk of developing colorectal cancer per 50 g/d increment (4).
- *Figure 7.1* shows the colon and rectal cancer cases attributable to processed meat intake in males and females.
- Overall, **0.8% of all cancers** (excluding NMSC) were attributable to high processed meat intake in Ireland in 2016. The estimated total of cancer cases attributable to processed meat intake in Ireland in 2016 was **173**. *Figure 7.2* presents the difference in cases and PAF for all cancer related to processed meat for males and females.

Fig 7.1 Male and female colon and rectum cancers attributable to processed meat intakes.



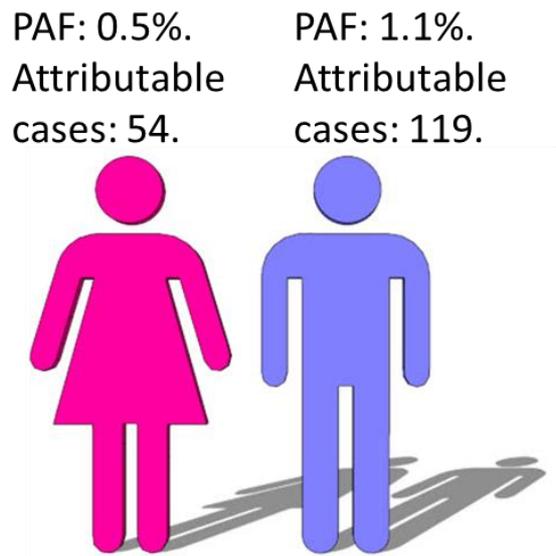


Fig 7.2. PAF% and attributable cases, males and females.

- The link between meat intake and cancer has been widely covered in the media in recent times, with processed meat being categorised as being group 1 carcinogens by IARC, i.e. in the same group as smoking and alcohol intake (2). Red meat has been deemed a ‘probable’ cause of cancer (or a Group 2a carcinogen) and therefore has not been included in this analysis. However, it is important to emphasise that IARC classifications describe the levels of **scientific confidence** that red and processed meat are linked to cancer but **not how much cancer they cause**.

How do these figures compare?

The PAFs for processed meat intake and cancer incidence in Ireland were similar to those reported in the UK and US; 1.5% and 0.8% respectively (5, 6).

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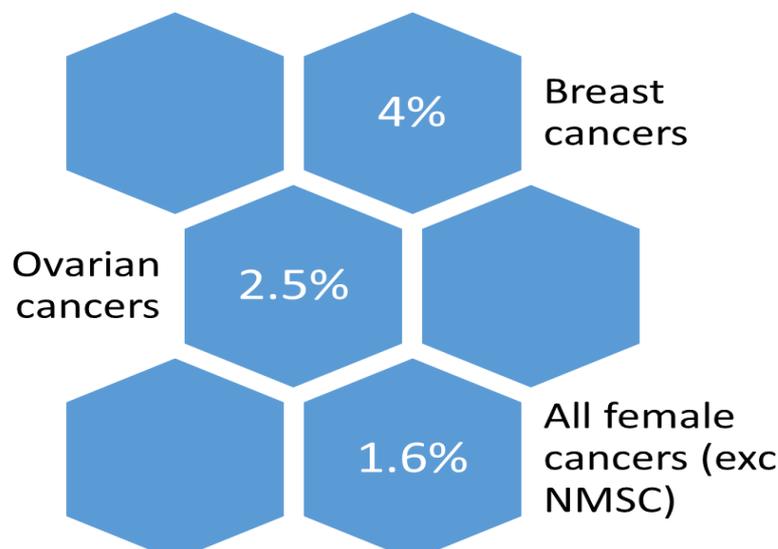
RISK FACTOR 8. HORMONAL REPLACEMENT THERAPY

- Hormonal replacement therapy (HRT) is used to replace the female hormones that are no longer produced as a result of the menopause or medical conditions associated with reduced circulating female hormones. This can improve quality of life by relieving many of the symptoms of hormonal insufficiency/ menopause. There is also evidence to suggest that HRT can reduce risk of colorectal cancer and osteoporosis (1).
- However, IARC report that there is sufficient evidence in humans for the carcinogenicity of combined oestrogen-progestogen menopausal therapy. HRT is associated with a small but measurable increased risk of cancer of the breast and of the endometrium (1).
- IARC indicate that hormone-receptor mediated responses are a likely mechanism for carcinogenesis by HRT. It is also thought that there is potential involvement of genotoxic effects of HRT or the

associated metabolic by-products including formation of DNA adducts and reactive oxygen species that damage DNA (1).

- It is important to consider that HRT covers a wide range of treatments and that different forms, as well as duration of treatment, are associated with different risks and benefits. Benefits include reduced risk of some malignancies, osteoporosis and some cardiovascular issues (2). This was not accounted for in this analysis and **the analyses did not seek to quantify the health benefits (including reducing incidence of some cancers) of HRT**. It is recommended that individuals concerned about their cancer risk should seek the advice of a healthcare professional in relation to the balance of risks and benefits of HRT.

Fig 8.1 HRT and female cancer



- Data from the Primary Care Reimbursement Service (PCRS) was obtained for 2006 and showed that 6.3% of women in the database were being prescribed some form of HRT.
- Research on the relative risks of current versus never users of HRT shows that current users are 43% more likely to develop ovarian cancer and 66% more likely to develop breast cancer (see methodology annex).
- Overall, **0.5% of all female cancers** (excluding NMSC) were attributable to HRT usage in Ireland in 2016. The estimated total of cancer cases attributable to HRT usage in Ireland in 2016 was **114**. See *Figure 8.1* for cancer type details.

How do these figures compare?

The PAFs for HRT usage and cancer incidence were reported in France and Australia as 1.4% and 1.1% respectively (3, 4). Analysis in Alberta, Canada, in which potentially prevented as well as attributable cancers were calculated, reported 2.7% of cancer being attributed to current usage of HRT and 0.3% of cancer incidence potentially prevented (5).

References

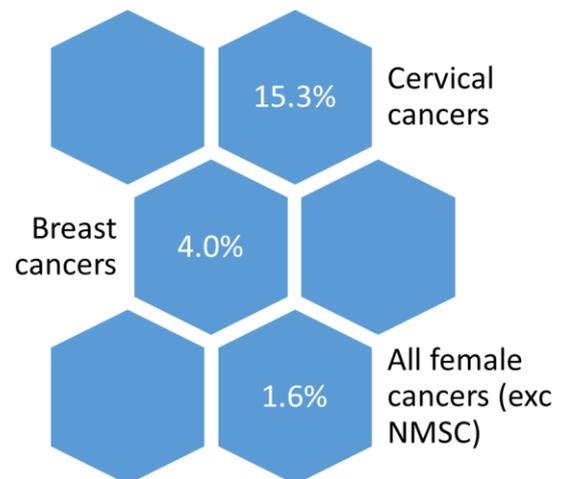
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RISK FACTOR 9. ORAL CONTRACEPTION

- IARC assess that there is sufficient evidence for the carcinogenicity of different types of oral contraceptives, including combined estrogen and progestogen oral contraceptives. Combined hormonal contraceptive use is associated with an increased risk of cancer of the breast and of the cervix for a period of time after use (1, 2).
- Oral contraceptives are also associated with a decreased risk of other cancer types, including ovarian, colorectal and endometrial, which is not accounted for in this report. It is likely that the net effect of cancer cases attributable to oral contraceptive usage is close to neutral (2, 3).
- The mechanisms through which oral contraceptives act as carcinogens are similar to those for HRT: through direct genotoxicity and receptor-mediated effects, including cell proliferation and differentiation (1).
- Data from the PCRS was obtained for 2006 and showed that 20% of women in the database were being prescribed oral contraceptives.
- Compared to women who have never used an oral contraceptive, current users are at a 90% and 21% higher risk of being diagnosed with cervical and breast cancers respectively (see methodology).
- Overall, **0.5% of all female cancers** (excluding NMSC) were attributable to oral contraceptive usage in Ireland in 2016. The estimate of total cancer cases attributable to oral contraceptive usage in Ireland in 2016 was **114**. See *Figure 9.1* for cancer type details.
- A more detailed analysis of oral contraceptive usage was carried out in Alberta, Canada in which potentially prevented, as well as attributable cancer cases were calculated. It was reported that 1.8% of

cancer was attributable to, and 4.3% was potentially prevented by, using oral contraceptive (3).

Fig 9.1 Oral contraceptives and female cancer



Note: Cervical cancer is largely attributable to HPV, however long-term use of oral contraceptives may increase the probability of the progression of HPV infection into cervical cancer. Therefore a proportion of cervical cancer is also attributable to women who contract HPV and are also taking certain types of oral contraceptives.

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RISK FACTOR 10. LACK OF PHYSICAL ACTIVITY

- The WCRF state there is convincing evidence that physical activity decreases the risk of colon cancer (1). They define physical activity as any movement that uses skeletal muscles and requires more energy than resting.
- There are a number of ways in which physical activity is thought to reduce colon cancer. Physical activity results in body fat reduction and may have a beneficial effect on colorectal cancer risk through a reduction in insulin resistance and inflammation (1).
- The 2007 SLAN report defined physical activity as low, moderate or high (see methodology annex for definitions). Overall, 71% of respondents had physical activity scores that fell within the moderate (47%) or high (24%) range (2).
- A 10% reduction in relative risk of colon cancer is observed in persons with moderate or high compared to low levels of physical activity (see methodology). Our methodology did not seek to quantify the numbers of cancers prevented by having the moderate or high activity lifestyles common in our society.
- 3% of colon cancer cases are attributable to physical inactivity in Ireland.
- Overall, the levels of inactivity in the SLAN report are associated with a **0.2% increased burden of all cancers** (excluding NMSC) in 2016. The estimate of total cancer cases attributable to physical inactivity in Ireland in 2016 was **38**. See *Figure 10.1* for difference between male and female incidence.

How do these figures compare?

The PAF for physical inactivity and cancer incidence in the UK was 0.5% (3).

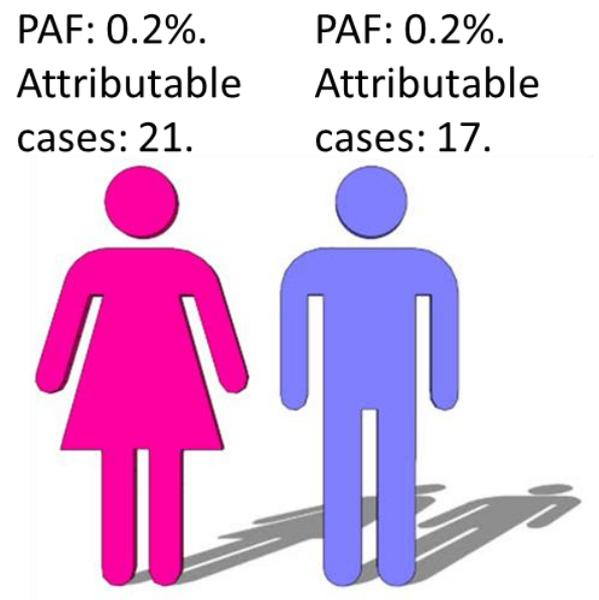


Fig 10.1. PAF% and attributable cases, males and females.

- The Health Service Executive Ireland recommend that adults get at least 30 minutes a day of moderate activity on 5 days a week (or 150 mins a week) (4).
- With 71% of our population having moderate or high levels of activity we would expect to see a rise in cancer numbers if these levels of activity were to significantly decline across the population over an extended period.
- Breast, rectal and endometrial cancer may be additional cancers included in future analysis for this risk factor, subject to clarification of the strength of evidence for the role of physical inactivity in these cancers. The promotion of physical activity is likely to be an effective strategy in the primary prevention of these commonly diagnosed cancer types.

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RISK FACTOR 11. FINE PARTICULATE AIR POLLUTION (PM_{2.5})

- When organic matter is burned, airborne particulate pollution is emitted. According to IARC, there is convincing evidence that long-term exposure to this air pollution causes lung cancer (1).
- Ambient air pollution may act as a carcinogen through mutagenicity, genotoxicity and male germ cell effects (1).
- The Environmental Protection Agency (EPA) measures air quality in Ireland. In 2006, the EPA measured fine particulate matter (PM_{2.5}), an indicator of man-made emissions, in Cork city only and reported the annual mean as 9 PM_{2.5} (2).
- Although the measurements represent Cork city rather than national exposure, the EPA have since started monitoring PM_{2.5} concentrations at nine different sites and in 2009 these measurements were similar across zones. All observed concentrations were below the EU annual limit value. See EPA reports for further details (3).
- The relative risk for lung cancer associated with PM_{2.5} is 1.09, i.e. there is a 9% increase in risk per 10 µg/m³ in exposure to PM_{2.5} (see methodology).
- 7.5% of lung cancer cases (after smoking is accounted for) in Ireland would be attributable to exposure to airborne PM_{2.5}.
- Overall, **0.2% of all cancer** (excluding NMSC) were attributable to PM_{2.5} exposure, in Ireland in 2016. The estimate of total cancer cases attributable to PM_{2.5} from pollution in Ireland in 2016 was **36**. See *Figure 11.1* for difference between male and female incidence.

How do these figures compare?

In relation to air pollution (fine particulate matter) and cancer incidence, France and the UK reported PAFs of 0.4% and 1% (4, 5).

PAF: 0.2%.
Attributable
cases: 17.



PAF: 0.2%.
Attributable
cases: 19.



Fig 11.1. PAF% and attributable cases, males and females.

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SCENARIO PROJECTIONS

SMOKING, OVERWEIGHT & OBESITY, & ALCOHOL

Projections of all cancer cases (excluding NMSC) attributable to smoking, overweight/obesity and alcohol intake were modelled to 2035.

Projections of cancer cases attributable to smoking.

- *Figure P.1* presents male and female projections to 2035 for all cancer cases (excluding NMSC) attributable to smoking. It should be noted that these projections do not include exposure to passive smoking and do not account for recent trends in the use of e-cigarettes, and further investigation will be required when more information becomes available.
- By 2035, it is estimated that, if smoking rates remain unchanged, 2,897 and 1,765 male and female cancer cases will be attributable annually to smoking. This represents a 78% increase for males and a 53% increase for females (68% increase overall) compared with 2016 caseloads attributable to smoking. In the 10-year period ending in 2035, it is estimated that a cumulative total of 42,336 cancer cases will be attributable to smoking.
- In relation to smoking, a target scenario was then modelled where the percentage of smokers will be reduced to 5% by 2025 based on “Tobacco Free Ireland 2025” goals (1).
- If the percentage of smokers in Ireland were reduced to 5% of the population, it is estimated there would be over 1,000 fewer cancer cases a year by 2035 as a result (*Figure P.1*), compared with caseloads attributable to smoking if smoking prevalence

remained unchanged. This would translate to a smaller increase (5% for males, 18% for females and 28% overall) in cancer incidence attributable to smoking, compared with the much larger increases expected if smoking prevalence remained unchanged.

Projections of cancer cases attributable to overweight and obesity.

- By 2035, it is estimated that 848 and 940 male and female cancer cases will be attributable to overweight and obesity yearly (*Figure P.2*). This represents a 43% increase for males and a 100% increase for females (69% increase overall) compared with 2016 caseloads attributable to overweight and obesity. In the 10-year period ending in 2035, it is estimated that 16,267 cancer cases will be attributable to these factors.
- In the case of BMI, we applied two scenarios; these were based on the prevalence of overweight and obesity being either reduced or increased by 5% each.
- If the percentages of individuals in Ireland who are overweight and obese both decreased by 5%, it is estimated that there would be a 21% increase for males and a 68% increase for females (42% increase overall) in numbers attributable to high BMI by

2035, compared with 2016 caseloads attributable to overweight and obesity (*Figure P.2*). This would be a substantially smaller increase in cases attributable to high BMI than if prevalence of high BMI remained unchanged.

- If the percentages of individuals in Ireland who are overweight and obese both increased by 5%, it is estimated that there would be a 65% increase for males and a 128% increase for females (93% increase overall) by 2035, compared with 2016 caseloads attributable to these factors (*Figure P.2*). This would be a substantially greater increase in cases attributable to high BMI than if prevalence of high BMI remained unchanged.

Projections of cancer cases attributable to alcohol intake.

- *Figure P.3* presents projected incidence of cancer attributed to alcohol intake.
- By 2035, it is estimated that 394 and 457 male and female cancer cases will be attributable to alcohol intake yearly at the current rate of consumption. This represents a 37% increase for males and a 110% increase for females (69% increase overall) compared with 2016 caseloads attributable to

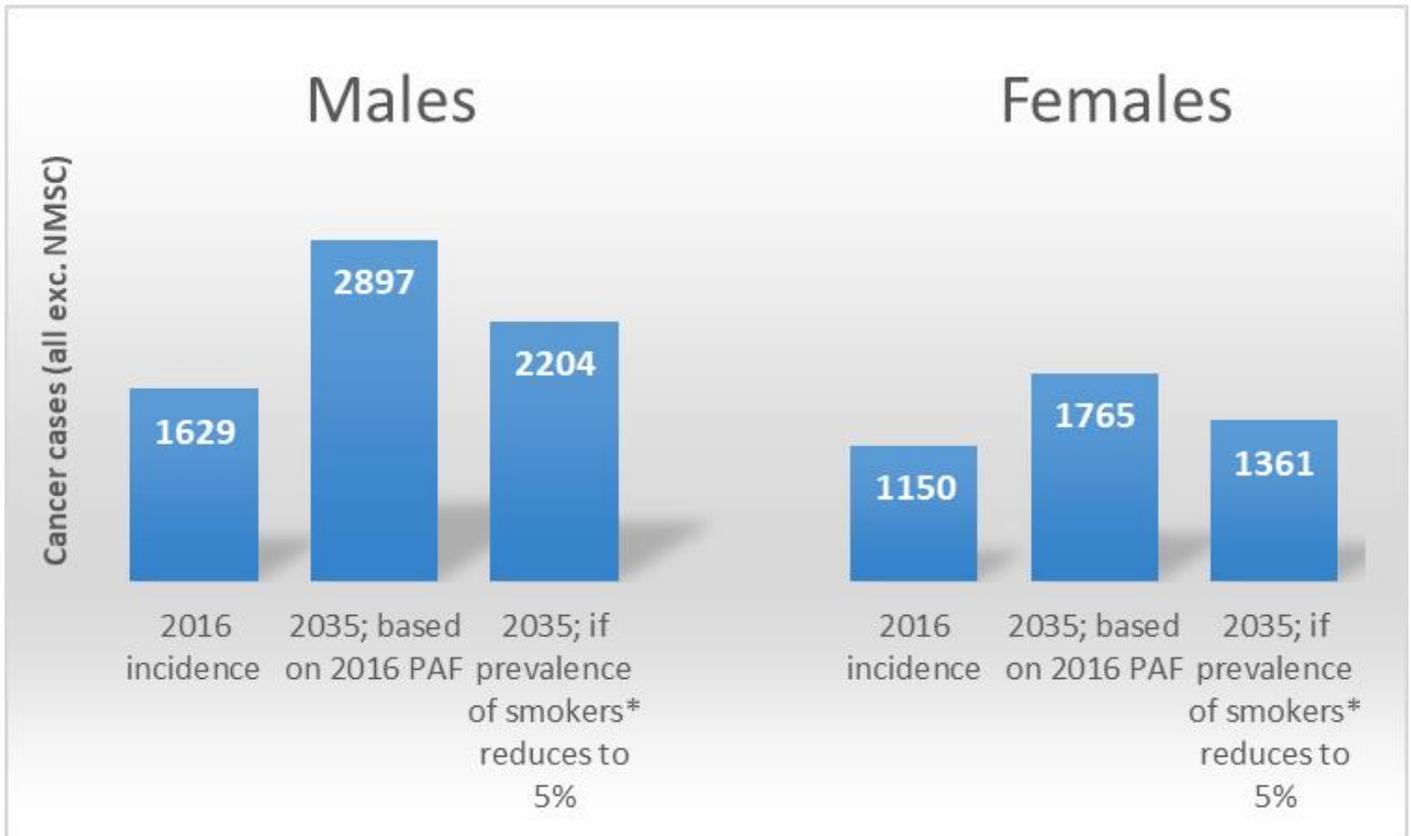
alcohol intake. In the 10-year period ending in 2035, it is estimated that 7,741 cancer cases will be attributable to alcohol intake.

- As well as projecting the cancer incidence attributable to alcohol intake with the current PAF, a scenario involving a decrease in the prevalence of moderate and heavy drinkers was also modelled, reflecting decreasing trends in alcohol usage (see methodology annex for details).
- If the percentages of individuals in Ireland who are moderate and heavy drinkers both decreased by 5%, it is estimated that there would be no increase (a 0.1% decrease) in alcohol-attributable cases for males but a 79% increase for females (34% increase overall) by 2035, compared with 2016 caseloads attributable to moderate or heavy alcohol consumption (*Figure P.3*). This would represent a substantial improvement over projections based on no change in alcohol consumption.

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Figure P.1. Cancer cases (all excluding NMSC) attributable to smoking in 2016 and in 2035, with current smoking PAF and the PAF if the percentage of current smokers was reduced to 5%, by sex.



*excludes ex-smokers

Figure P.2. Cancer cases (all excluding NMSC) attributable to overweight and obesity in 2016 and in 2035, with current PAF and PAF if the prevalence of overweight and obesity was either reduced or increased by 5%, by sex.

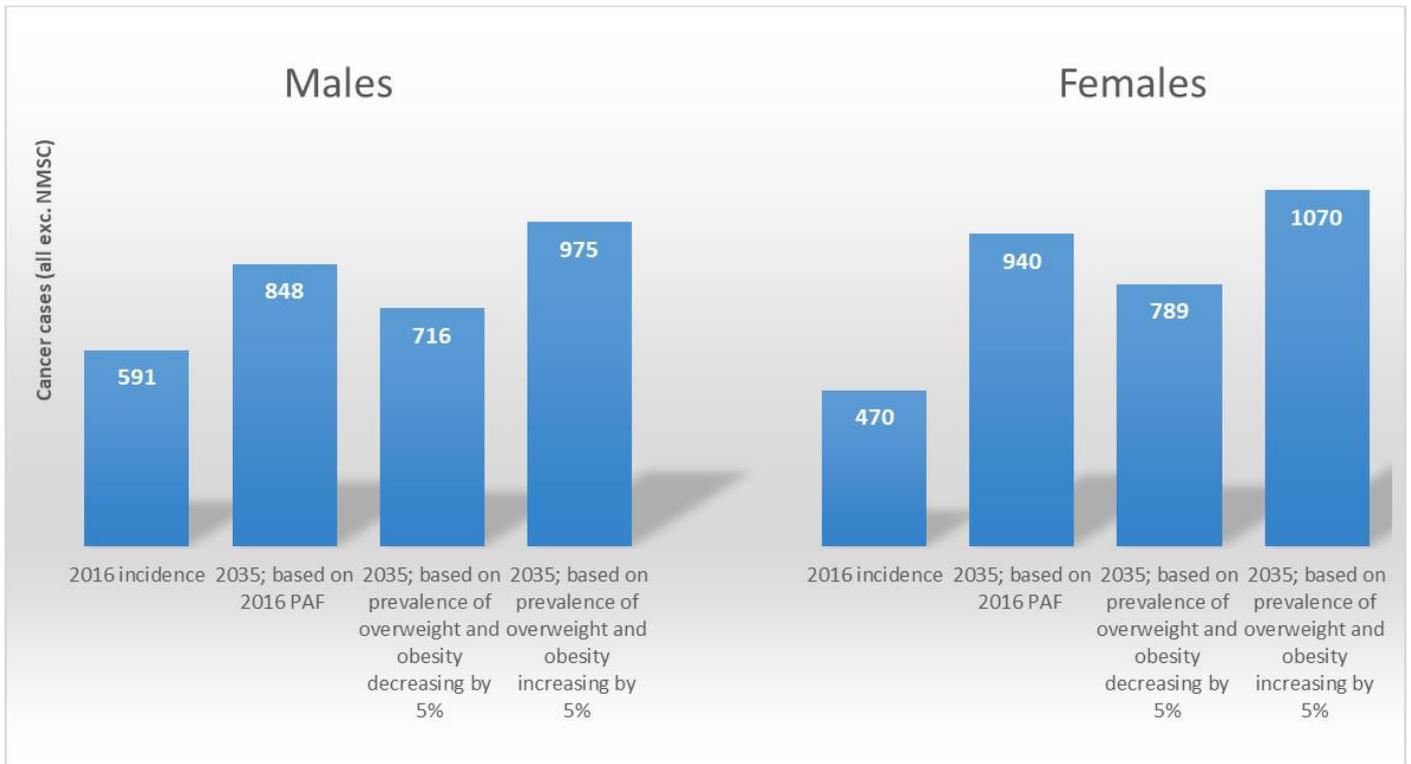
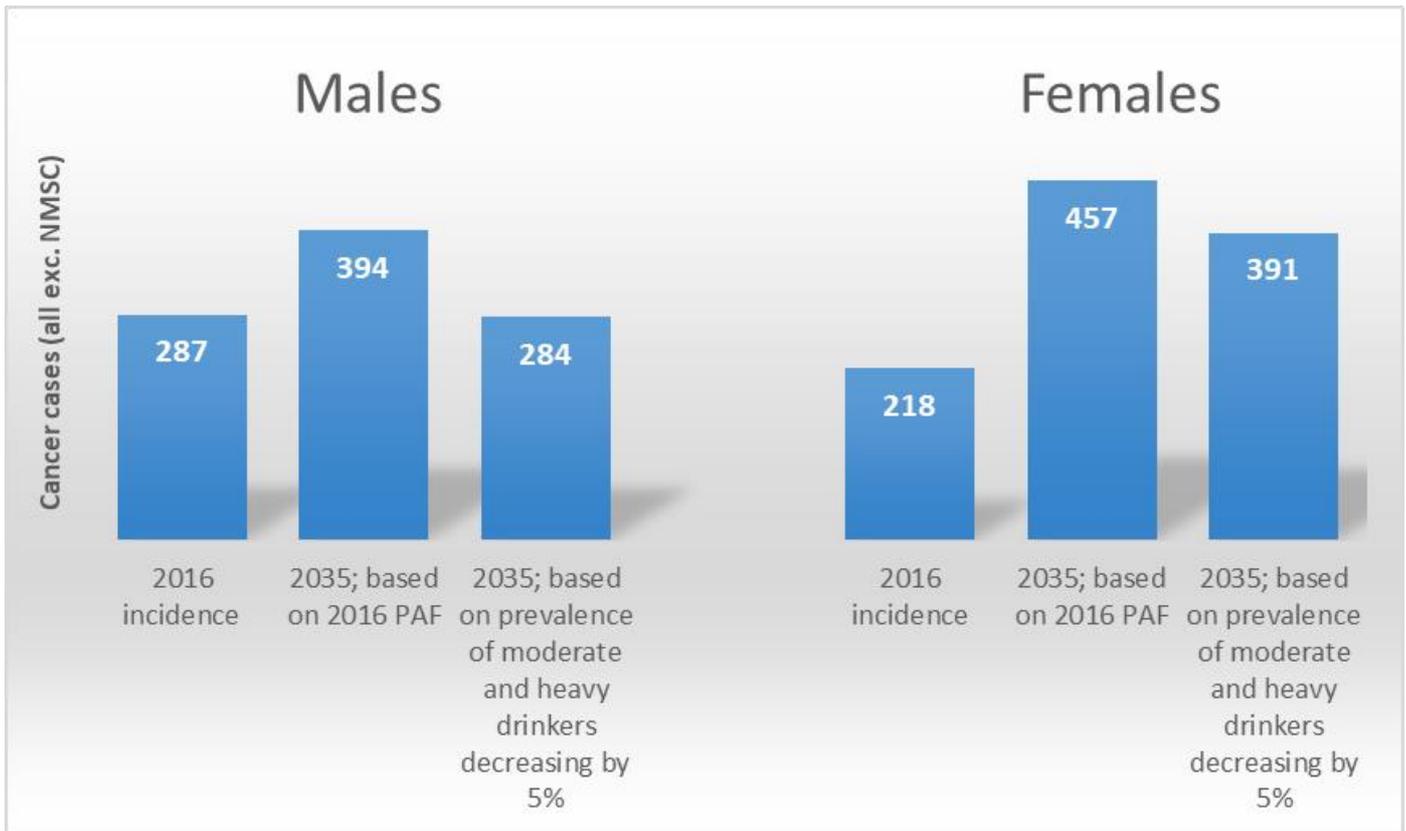


Figure P.3. Cancer cases (all excluding NMSC) attributable to alcohol intake in 2016 and in 2035, with current PAF and PAF if the prevalence of moderate and heavy alcohol intake was reduced by 5%, by sex.



KEY DISCUSSION POINTS

Summary

- In 2016, an estimated 29.3% (6,238) of all cancer cases (excluding NMSC) were attributable to the 11 modifiable risk factors examined in this study;
 - Smoking
 - Infection
 - Overweight and obesity
 - Alcohol intake
 - Single-episode sunburn, and sunbed usage
 - Ionizing radiation
 - Processed meat intake
 - Oral contraceptives
 - Hormone replacement therapy
 - Lack of physical activity
 - Air pollution (due to fine particulate matter).
- UK based research on the proportion of cancer attributable to modifiable risk factors reported 37.7% of cancer in 2015 as being attributable to 14 different modifiable lifestyle risk factors (1), so our findings are similar given our narrower range of focus on factors and the conservative, high stringency of the attributable fractions we employed.
- The United States reported 42% of cancer as being potentially preventable, with the higher number largely being due to different inclusion criteria utilised (2). That study included additional dietary factors, such as low fruit and vegetables, low fibre, low calcium, and consumption of red meat.
- Smoking, overweight and obesity, and infections were the top 3 risk factors in Ireland, together accounting for about 21% of all cancers.
- Smoking (including passive smoking in the home) was the risk factor accounting for the highest attributable proportion of all cancer (excluding NMSC) cases, at 13%. Brown et al. reported 14.6% and 15.1% of cancer as being attributable to smoking in 2015 in Northern Ireland and the wider UK respectively (1).
- The estimates we have arrived at are most likely quite conservative. Although the 10-year lag period has been determined as most suitable for use in evaluating burden of disease, there is evidence that a longer latency period is required to determine the cancer incidence attributable to some factors, such as tobacco smoking. As prevalence of smoking is decreasing, the chosen lag period may yield an underestimate. However, the impact may be minimal, for example the UK reported a difference of only 1 percentage point when using 20-year latency compared with 10 year latency period (1). This supports the use of higher quality, more recent data with a 10-year latency period in Ireland.
- 5.0% of cancer cases (excluding NMSC) were attributable to being overweight or obese; this equates to 1,061 cancer cases in Ireland in 2016. Brown et al. reported that 6.3% of cancer incidence in the UK was attributable to overweight and obesity (1).
- A number of carcinogenic infection types were grouped together, and overall 3.6% of cancer (excluding NMSC) incidence in Ireland was attributable to these infections. In the UK, 3.6% of cancer incidence in 2015 was reported attributable to infection (1). The burden of cancer attributable to infection has previously been reported as higher in Ireland compared to the UK (3). It should be noted that for certain infection types, including *H. pylori*, there is no adequate data on prevalence in Ireland. As a result, either pre-calculated PAFs or data from

Northern Ireland were used as an alternative. Further national information on the prevalence of infection would strengthen our understanding of this evidence.

- Public awareness of modifiable risk factors for cancer needs to be addressed. According to recent Irish surveys, only 32% of people are aware that obesity is a risk factor for cancer (4), 75% of Irish adults don't know what HPV is and 56% of Irish adults are not aware that HPV infections can cause cancer (5).
- Lung cancer had the highest number of cases attributable to modifiable risk factors in both males and females, followed by colon and stomach cancer in males and breast and cervical cancer in females. This is consistent with international findings (1, 2).
- The differences between males and females in cancer cases attributable to modifiable risk factors have been highlighted in each risk factor section, with males having higher PAFs for smoking and processed meat intake, and females having higher PAFs for overweight and obesity, infection and alcohol intake.
- These are largely modifiable risk factors meaning that at least 29.3% of cancer incidence in Ireland is potentially preventable. The prevention of cancer should be the first step in cancer control, in terms of reducing the burden on both patients and health services (6).
- It is important to consider that this 29.3% is an underestimate of preventable cancer in Ireland, for example:
 - The risk associated with occupation was not accounted for here and should be examined in future research. In the UK, 3.8% of cancer cases were attributable to occupation-related risk.
 - Everyday exposure to ultraviolet radiation (UVR) was not included; only sunburn history (single episode) and sunbed usage.
- Between 2026 and 2035 (inclusive), it is estimated that a cumulative total of 66,343 cancer cases will be attributable to smoking, overweight and obesity,

and alcohol intake if prevalence of these risk factors remains unchanged.

- Assuming prevalence remains the same, it is estimated that in 2035 there will be 4,661 cancer cases attributable to smoking, 1,788 attributable to overweight and obesity, and 851 attributable to alcohol intake.
- Several of the risk factors in this report are associated with not only cancer but a range of other diseases, including heart disease, cerebrovascular disease, diabetes and chronic obstructive pulmonary disease. Therefore policies to reduce the prevalence of these modifiable risk factors should consider the wider impact on public health.

Limitations and considerations

- PAF estimates are dependent on the quality of the data from which they are calculated. When selecting the relative risk for each cancer and risk-factor combination, differences in cancer risk among subpopulations need to be considered.
- Furthermore, data on exposure to risk factors come from multiple sources and not all of these may be nationally representative. There needs to be more comprehensive and routinely collected data on exposure to modifiable health-risk factors in Ireland. The routine monitoring of health behaviours at a population level is necessary to plan and evaluate the impact of effective cancer prevention strategies.
- The limitation above is a particular issue in relation to prevalence of infection types. As described previously, a variety of information sources were used as substitutes in the absence of nationally representative data including Northern Ireland data for *H. pylori* and pre-calculated PAFs for HPV and EBV (as per Brown et al. (1)). The data used to estimate *H. pylori* prevalence is from the 1980s and therefore to overcome this limitation we aimed to reflect changes in treatment and prevalence over time by applying an annual mean decrease based on European trends. See methodology annex for further details.

- The biological latency period between exposure to a risk factor and development of cancer is another important consideration. This is sometimes unknown and there can be large variation in estimates depending on the risk factor and cancer type. Given the lack of data on this and in order to be consistent with other analysis in this area, a 10-year lag time was selected for all risk factors (1).
- Estimates of PAFs in this report are conservative as we used stringent criteria, requiring un-ambiguous consensus assertions by relevant professional bodies as to carcinogenicity, and calculations were based only on cancer / risk-factor combinations with the highest levels of evidence (“convincing” or “sufficient”).
- These estimates are also conservative due to the risks associated with occupation and everyday sun exposure not being accounted for here, as well as issues in determining latency periods, which should be addressed in future investigations.
- In 2013, Laffoy et al. published research on cancer incidence due to alcohol intake in Ireland and estimated PAFs of 4.7% in males and 4.2% in females (7). The differences between the PAFs reported here and those previously published are explained by methodological differences. For example, Laffoy et al. used SLAN data and adjusted for self-reporting. In this analysis, NANS data and updated relative risks based on a 2015 meta-analysis were applied. Furthermore, differences in the cancer site inclusion criteria between the two studies also contribute, but to a lesser extent, to differences between these studies in their findings re alcohol intake.
- This analysis reports 0.2% of all cancer (excluding NMSC) as attributable to physical inactivity. This is a conservative estimate and is lower than the UK figure of 0.5% (1). A more sophisticated analysis on physical inactivity is warranted in which factors such as the time and intensity of physical activity are also taken into account. It is also important to point out that these figures are based on the majority of our population being moderately or highly active (known to reduce the incidence of a number of malignancies). Hence, if activity rates declined, we might expect a disproportionate increase in cancer rates commensurate with reduction in the anti-carcinogenic effect of this type of lifestyle.
- This report focuses on the fraction of cancer attributable to sunburn history (ever sunburned) and sunbed usage only, and does not include the fraction attributable to everyday sun exposure, due to lack of data on Irish sun exposure behaviours. Given that over-exposure to the sun is the single biggest cause of cancer (if the generally less dangerous non-melanoma skin cancers are also included), further analysis needs to be undertaken to establish its true impact.
- This analysis only includes information on risk factors increasing the risk of cancer and does not account for how certain risk factors, such as oral contraceptive and HRT usage, can potentially reduce certain cancer types and other disease.
- The analysis does not attempt to take into account the potential cancer-causing synergies of multiple factors taken together. For example, smoking and HPV infection synergise to increase the likelihood of head and neck cancers. Smoking and radon gas exposure synergise to give greater likelihood of lung cancer than simply adding the PAFs for each factor together.
- Subgroup analysis in different socio-demographic groups is warranted due to the different rates of smoking, alcohol use and obesity evident in different communities. However, this is not possible at this time due to lack of relevant information for many of the risk factors included in this analysis. Prevention strategies need to be mindful of various groups in our society that face greater burdens from particular types of cancer.
- There are also likely to be differences between rural and urban areas, which should be considered in future investigations on risk factor prevalence.
- This analysis relates to primary cancer incidence in Ireland, and there is no estimate for the contribution of these modifiable risk factors to the risk of cancer recurrence.

Strengths

- Cancer type and modifiable risk factors were included using definitions by IARC or WCRF as having “sufficient” (IARC) or “convincing” (WCRF) evidence of a causal association.
- The approach taken is consistent across all risk factors and all cancer types and can be replicated in future analysis.
- The analysis is comparable to similar work carried out in different countries, including the UK (1).
- This analysis has involved the use of NCRI data on population-level cancer incidence. This is high-quality, complete data (8).
- The risk factors selected are largely modifiable and amenable to strategic policy responses and initiatives.
- This analysis provides context-specific evidence; such information has not previously been available in Ireland.
- Cancer cases (excluding NMSC) attributable to smoking (excluding passive smoking), overweight and obesity, and alcohol intake were modelled to 2035. These projections should be considered by policymakers and there needs to be an effort to ensure that the projected increases are not realised.

Recommendations

- Out of the 11 risk factors examined, smoking, overweight and obesity, and infection are the biggest risk factors for cancer incidence in Ireland. These risk factors need to continue to be targeted by public health representatives and policymakers.
- The findings in this report should be used for future health-related policy planning. Efforts to ensure that projected increases in cancer incidence are not realised are essential.
- Comprehensive and routine collection of data on exposure to risk factors in Ireland needs to be considered in the future.

- Analyses in this report should be repeated in future years to ensure regular monitoring and to assess the impact of policy change and intervention on public health outcomes.
- Research studies on specific risk factors using more sophisticated methodology should be considered both locally and internationally.
- Future work in this area should examine outcomes including the impact on mortality, quality of life, etc. in addition to cancer incidence.
- The impact of risk factors on quality of life should be considered in future analyses. This is an important question, as cancer is increasingly described as a chronic disease, and impacts on quality of life will depend on the specific types of cancer and treatments involved.
- Economic impacts of modifiable risk factors for cancer should also be considered. The economic burden of cancer for the health services, patients and their families, and society at large are substantial. This burden will likely increase in the coming years as novel, more expensive treatments become available and the number of people living with and beyond cancer increases. The NCRI will be compiling a follow-up report estimating the economic burden of cancer in Ireland attributable to modifiable risk factors, and that report’s findings should be considered by policymakers.

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