

## **Cancer Incidence and Mortality Due to Inadequate Physical Activity**

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### **Abstract**

#### **Aim**

Inadequate physical activity increases risk of specific cancers. This study aimed to calculate the Population Attributable Fraction (PAF) of inadequate physical activity and estimate cancer burden due to this exposure among adults in Ireland from 2011-2015.

#### **Methods**

A literature review identified relative risks for inadequate physical activity and cancer. Prevalence of this exposure in Ireland was estimated using a nationally representative survey. The PAF was calculated and applied to Irish cancer incidence and mortality data (2011-2015).

#### **Results**

Inadequate physical activity in Ireland resulted in approximately 1,500 cancer cases (5% of total) and 500 deaths (6% of total) in specific cancer sites (colorectal, breast, and endometrial) from 2011-2015. Women were disproportionately affected.

#### **Conclusion**

Given the harm due to inadequate physical activity, urgent actions are needed to inform the public and to strengthen policy and strategy in Ireland to address this problem.

### **Introduction**

There are almost 24,000 incident invasive cancers (excluding non-melanoma skin cancer) and over 9,000 cancer deaths per year in Ireland<sup>1</sup>. The number of new cases annually is estimated to double by 2045<sup>2</sup>. Changing demographics, including an ageing population, are principal drivers of the increase.

It is estimated that 30% to 50% of all cancers are preventable<sup>3</sup>. There is significant evidence that physical activity (PA) protects against several cancers<sup>4</sup>. Biological mechanisms by which PA may reduce cancer risk include promotion of endogenous steroid hormone metabolism, decreasing circulation of oestrogens and androgens, reduction of insulin resistance and long-term inflammation, and improved immune function.

At a cellular level these processes encourage beneficial effects such as increased apoptosis, reduced proliferation (including in oestrogen sensitive tissues), and less genome instability. As body weight and PA are related, PA may also reduce cancer risk through lowering adiposity.

The National Cancer Strategy 2017-2026 highlights cancer prevention as a key priority in Ireland<sup>5</sup>. Inadequate PA is a known exposure associated with risk of developing specific cancers. This is the first study to calculate the Population Attributable Fraction (PAF) of inadequate PA on cancer incidence and mortality in Ireland. The PAF is an epidemiological measure commonly used to assess the impact of exposures at a population level. Findings will improve understanding of the cancer burden in Ireland due to inadequate PA.

## Methods

The PAF for inadequate PA was calculated using relative risks (RRs) from meta-analyses identified in a literature review, data on prevalence of inadequate PA in the population in Ireland, and cancer incidence and mortality data in Ireland from 2011-2015.

A comprehensive literature search was performed in PubMed and the Cochrane library to identify studies examining inadequate PA as a cancer risk. This was conducted using a structured approach based on the 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>6</sup>. Systematic reviews and meta-analyses of epidemiological studies were used as the source of RRs. The Critical Appraisal Skills Programme (CASP) tool for systematic reviews was employed to guide the literature appraisal<sup>7</sup>.

The literature review included meta-analyses and systematic reviews on physical activity and incidence of cancer. It excluded primary research articles, reviews on non-Caucasian populations, articles on paediatric cancer, articles where the exposure measured was sedentary time independent of physical activity and articles that did not include a RR based on appropriate dose-response thresholds/categories. Medical Subject Heading (MeSH) terms neoplasm, physical exertion, and exercise were included and the key words breast, colorectal, endometrial, tumour, physical exercise, physical activity, and physical exertion.

Full search terms are detailed as follows: ((Neoplasm[MeSH Terms] OR cancer\*[Title/Abstract] OR neoplasm\*[Title/Abstract] OR neoplasia?[Title/Abstract] OR tumour?[Title/Abstract] OR tumor?[Title/Abstract] OR malignanc\*[Title/Abstract])) AND (((physical exertion[MeSH Terms] OR exercise[MeSH Terms] OR physical activ\*[Title/Abstract] OR physical inactiv\*[Title/Abstract] OR physical exercise[Title/Abstract] OR physical movement[Title/Abstract] OR physical exertion[Title/Abstract] OR physical fitness[Title/Abstract] OR sedentary[Title/Abstract])))

The following limits were applied: publication in English, studies on humans, studies published between 2008 and 2018, and study types which were meta-analyses and systematic reviews.

The key measure extracted from the literature review was the RR per cancer, per PA category (Table 1).

**Table 1: Summary of selected relative risks for cancers associated with inadequate physical activity**

Cancer type	ICD-10 Code	Article source/ year	Measurement of exposure	Category of exposure	Adequate PA RR (95%CI)
Colorectal (both sexes)	C18- C20	Kyu (2016) <sup>8</sup>	Total PA in MET minutes/week	600-3999 Reference category: <600	0.90 (0.85-0.95)
Breast (female)	C50	Kyu (2016) <sup>8</sup>	Total PA in MET minutes/week	600-3999 Reference category: <600	0.97 (0.94-1.00)
Endometrial	C54.1	Schmid (2015) <sup>9</sup>	MET-hours per week of recreational PA	9-20 Reference category: <3	0.79 (0.64-0.98)

*ICD-10=International Classification of Disease-10; PA=physical activity; RR=Relative Risk; 95%CI=95% Confidence Interval; MET=Metabolic Equivalent*

Data on inadequate PA prevalence in the Irish population was determined from the Survey of Lifestyle, Attitudes and Nutrition (SLÁN) 2007, a robust nationally representative dataset<sup>10</sup>. Previous literature identified seven to ten years as an appropriate latency period<sup>11,12</sup> between time of exposure and development of an attributable cancer. The use of SLÁN 2007 data allows a lag time of four to eight years. However, exposure to inadequate PA is relatively stable over time and was likely similar over preceding years.

A summary continuous variable of total PA across all domains in life (including leisure time, domestic activities, occupational, and transport-related) in Metabolic Equivalent (MET)-minutes per week (moderate- and vigorous-intensity) was produced, enabling calculation of the population proportions that were adequately ( $\geq 600$  MET-minutes/week) and inadequately physically active ( $< 600$  MET-minutes/week) in line with World Health Organization (WHO)<sup>13</sup>/Irish PA recommendations<sup>14</sup> and the colorectal and breast cancer RR categories (Table 1). METs express intensity of PA. A MET is the ratio of a person's working metabolic rate relative to their resting metabolic rate. One MET is defined as the energy expenditure of sitting quietly, equating to a caloric consumption of 1 kilocalorie/kilogram/hour<sup>15</sup>. The RR for endometrial cancer identified from the literature used 9-20 MET-hours/week of recreational PA as its adequate PA threshold. As it was not possible to calculate recreational PA alone using SLÁN 2007 data the higher threshold of 20 MET-hours (1,200 MET-minutes) of total PA (all domains) was used as a proxy in estimates relevant to endometrial cancer.

Cancer incidence and mortality data were requested from the National Cancer Registry Ireland (NCRI) and the Central Statistics Office (CSO), respectively<sup>16,17</sup>. The most recent data available (2011-2015) were requested by sex and five-year age groups for the identified cancers using International Statistical Classification of Diseases and Related Health Problems codes<sup>18</sup>. Age groups less than 20-years-old were not included as the PAF calculation comprised only adults.

The following standard formula, used in international literature and appropriate to the available RR data in this study, was employed to estimate the PAF<sup>19</sup>:

$$PAF = \frac{\sum(p_x \times ERR_x)}{1 + \sum(p_x \times ERR_x)}$$

**Figure 1: Standard PAF formula**

Where  $p_x$  is the proportion of the population who are inadequately physically active and  $ERR$  is the excess relative risk associated with being inadequately physically active. The  $ERR$  of being inadequately physically active was calculated as  $(1/RR) - 1$ .

The fractions of incident cancer cases and deaths due to insufficient PA for each relevant cancer type were then calculated by applying the PAF to the incidence and mortality data for 2011-2015, for both sexes where appropriate, in five-yearly age groups.

Sensitivity analysis was conducted by applying 95% confidence intervals for the RRs for the cancers selected from the literature review.

## Results

The PAF for inadequate PA on cancer incidence and mortality in Ireland over a five-year period (2011-2015) was calculated by sex, five-year age grouping, and cancer type. Results of attributable incident cancer burden stratified by cancer type and sex are presented in Table 2. Results of attributable mortality burden stratified by cancer type and sex are presented in Table 3. All data below apply to persons aged 20 years and older.

### *Cancer incidence attributable to inadequate PA, 2011-2015*

In total, 1,556 incident cancers (95%CI 479-2,619) from 2011-2015 were estimated to be attributable to inadequate PA. This corresponded to 5% (95%CI 2%-9%) of new diagnoses in relevant cancer types in the study period.

From 2011-2015, 500 (95%CI 243-783) and 379 (95%CI 185-592) incident colorectal cancers were estimated to be preventable in men and women, respectively. This equated to 7% of all colorectal cancers in both sexes.

Of 14,710 breast cancer cases, 321 (95%CI 19-619) were estimated to be preventable with adequate PA. This equated to 2% (95%CI 0.1%-4%) of all breast cancers. Of 1,953 endometrial cancers, 356 (95%CI 32-625) were estimated to be preventable with adequate PA. This corresponded to 18% (95%CI 2%-32%) of the total number of incident endometrial cancers.

**Table 2: Incident cancers attributable to inadequate physical activity, 2011-2015**

<b>Cancer type</b>	<b>Number of incident cancers, per cancer type, 2011-2015</b>	<b>Number of incident cancers attributable to inadequate PA, 2011-2015 (95%CI)</b>	<b>Proportion (%) of incident cancers attributable to inadequate PA, 2011-2015 (95%CI)</b>
<b>Male</b>			
Colorectal	7,417	500 (243-783)	6.7 (3.3-10.6)
<b>Total male</b>	7,417	500 (243-783)	6.7 (3.3-10.6)
<b>Female</b>			
Colorectal	5,148	379 (185-592)	7.4 (3.6-11.5)
Breast	14,710	321 (19-619)	2.2 (0.1-4.2)
Endometrial	1,953	356 (32-625)	18.2 (1.6-32.0)
<b>Total female</b>	21,811	1,056 (236-1,836)	4.8 (1.1-8.4)
<b>Total (both sexes)</b>	29,228	1,556 (479-2,619)	5.3 (1.6-9.0)

*PA=physical activity; 95%CI=95% Confidence Interval*

*Source: Incidence data - NCRI*

#### *Cancer mortality attributable to inadequate PA, 2011-2015*

In total, 534 (95%CI 193-876) deaths occurred due to cancers attributable to inadequate PA, equating to 6% (95%CI 2%-10%) of all deaths in relevant cancer types.

In 2011-2015, 210 (95%CI 102-328) and 162 (95%CI 79-251) colorectal cancer deaths were estimated to be preventable in men and women, respectively. This equated to 7% (95%CI 4%-11%) and 8% (95%CI 4%-12%) of all colorectal cancers in men and women, respectively. Of 3,496 female breast cancer deaths, 85 (95%CI 5-163) were estimated to be preventable with adequate PA. This corresponded to 2% (95%CI 0.1%-5%) of all breast cancer mortality. Of 407 endometrial cancer deaths, 77 (95%CI 7-134) were estimated to be preventable with adequate PA, equating to 19% (95%CI 2%-33%) of total endometrial cancer mortality.

**Table 3: Cancer mortality attributable to inadequate PA, 2011-2015**

<b>Cancer type</b>	<b>Number of cancer deaths, per cancer type, 2011-2015</b>	<b>Number of cancer deaths attributable to inadequate PA, 2011-2015 (95%CI)</b>	<b>Proportion (%) of cancer deaths attributable to inadequate PA, 2011-2015 (95%CI)</b>
<b>Male</b>			
Colorectal	2,934	210 (102-328)	7.2 (3.5-11.2)
<b>Total male</b>	2,934	210 (102-328)	7.2 (3.5-11.2)
<b>Female</b>			
Colorectal	2,070	162 (79-251)	7.8 (3.8-12.1)
Breast	3,496	85 (5-163)	2.4 (0.1-4.7)
Endometrial	407	77 (7-134)	18.9 (1.7-32.9)
<b>Total female</b>	5,973	324 (91-548)	5.4 (1.5-9.2)
<b>Total (both sexes)</b>	8,907	534 (193-876)	6.0 (2.2-9.8)

*PA=physical activity; 95%CI=95% Confidence Interval*

*Source: Mortality data - CSO*

## **Discussion**

The key study findings were that in the five-year period, 2011-2015, over 1,500 cancer cases and 500 deaths in Ireland can be attributed to inadequate PA. This equated to approximately six new diagnoses and two deaths from cancer every week. Women were disproportionately affected. Amongst women it was estimated over 1,000 incident cases and 300 deaths were potentially preventable, compared with 500 incident cases and more than 200 deaths in men.

It is predicted, based on demographic changes, that annual breast cancer incidence will increase by over 60% by 2045<sup>2</sup>. In total, this study found that 2% of both incident cases and deaths from female breast cancer in 2011-2015 were potentially attributable to inadequate PA. This equated to over 300 potentially preventable incident cancers and 80 deaths in the relevant time period which underscores the importance of this avoidable exposure in the female population.

The RRs for colorectal and breast cancer identified in the literature review were measured against the WHO/national recommendations on PA (i.e. individuals should complete at least 600 MET-minutes per week of moderate and/or vigorous PA). This study found that the majority of cancer burden attributable to lack of PA was related to these cancers. The results also indicated that more than 350 endometrial cancer diagnoses and 70 deaths were potentially due to lack of PA.

This equated to an attributable incident cancer burden of 18% for endometrial cancer, compared with 2% for female breast cancer and 7% for colorectal cancer in both sexes. The higher burden for endometrial cancer should, however, be interpreted with a degree of caution. The estimates for endometrial cancer were calculated using a RR that was based on the female population achieving between 9-20 MET-hours per week of recreational PA, a higher threshold than recommended in WHO/national guidance. As it was not possible to calculate recreational PA using SLÁN 2007 data, the upper threshold of 20 MET-hours (1,200 MET-minutes) of total PA (all domains) per week was used instead, as a proxy to produce the estimate. This higher threshold was selected on the assumption that those who completed this higher level of total PA would also have reached 9-20 MET-hours of weekly recreational PA.

PAF calculations are subject to certain assumptions and limitations, and these therefore apply to this study too. The PAF calculation depends on the accuracy of the RRs from the literature and the population exposure data. As the primary study exposure data were predominantly self-reported this could have led to the introduction of bias through misclassification of PA domains or inaccuracy in recall of estimated frequency, duration or intensity by respondents potentially underestimating the role of physical activity in reducing cancer risk. There was also some variability in the types and categories of PA measurement across the primary studies included in the meta-analyses. Despite this variation, heterogeneity of the study outcomes in the meta-analyses included in the PAF was moderate, or lower, indicating consistency across study results. Although the selected meta-analyses included primary papers which adjusted for the most important covariates, such as age and Body Mass Index, there is potential for some residual confounding effect. Specifically, it is acknowledged that body weight and PA are related. Although excess body weight (as a risk factor for similar cancer types) was adjusted for in many of the primary studies it is possible there may be some overlap in attributable cancer burden with lack of PA.

Population surveys indicate levels of adequate PA have increased in Ireland over the last decade (e.g. 24% in SLÁN 2007 to 32% in Healthy Ireland 2015)<sup>10,20</sup>. If this increase in PA represents a sustained trend, the attributable cancer burden (as a proportion) may slightly reduce in the future. However, given two-thirds of the population remain inadequately physically active it is expected that the attributable cancer burden in Ireland will remain substantial. In addition, the growing and ageing population is likely to contribute considerably to actual case numbers (even if the attributable proportion reduces) – therefore from both an individual and a service delivery perspective it remains crucial that all appropriate preventive measures are implemented to further reduce this burden.

Inadequate PA is a modifiable risk factor. It is important that the general public are made fully aware of this risk and are appropriately supported in achieving higher levels of PA. Increasing PA is a whole of society issue and is best addressed through a cross-sectoral approach enshrined within the national framework on health and wellbeing, Healthy Ireland<sup>21</sup>. Effective implementation of healthy living initiatives such as the National Physical Activity Plan<sup>22</sup>, the National Obesity Policy and Action Plan<sup>23</sup> and the Healthy Eating and Active Living Programme<sup>24</sup> will support individuals to achieve higher levels of PA in their daily lives.

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**Declaration of Conflicts of Interest:**

The authors have declared that they have no conflicts of interest in this work.

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