Epidemiology of cancer-related weight loss and sarcopenia in the UK and Ireland: incidence, prevalence, and clinical impact

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Abstract

Background  Weight loss (WL) and sarcopenia are associated with negative oncological outcomes including poor treatment tolerance, decreased quality of life, and reduced survival. The number of patients affected by sarcopenia and WL in Ireland and the UK is unknown.

Methods  A systematic review was undertaken to determine median rate of WL > 5% and computed tomography-diagnosed sarcopenia in oncology populations. Gaps in the literature were supplemented using local data, collected as part of a 5 year prospective study. Rates of WL and sarcopenia in the population were extrapolated from these data based on incidence and prevalence of each cancer as per national cancer registries.

Results  We estimated that across Ireland and the UK, 128 892 cancer patients (34%) are affected by WL > 5% annually (121 641 UK; 7251 Ireland) and there are 133 707 annual cases of sarcopenia in cancer patients (35%) (126 265 UK; 7442 Ireland). Furthermore, we estimate that there are 716 124 and 771 589 cancer survivors with history of WL > 5% or sarcopenia, respectively.

Conclusions  Large numbers of patients are affected by cancer-related malnutrition. Given the impact of malnutrition on oncological outcomes and long-term frailty, there is an urgent need to improve access to cancer nutrition care.

Keywords  Malnutrition; Cancer; Sarcopenia; Weight loss; Body composition; Epidemiology

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Background

Cancer cachexia (CC) is a multifactorial syndrome characterized by weight loss (WL) (muscle loss with or without fat loss) and anorexia on a background of inflammation.1 CC is known to be common in oncology populations and is associated with negative clinical outcomes including poor tolerance to treatment, decreased quality of life (QoL), and reduced survival.2 As well as clinical and social outcomes of relevance to the patient, the cost of disease-related malnutrition to the health service is significant.3,4

Many studies have explored the impact of CC, as a condition both in its own right and in terms of its components, WL and sarcopenia. A recent systematic review, which included 35 studies with a cumulative 6894 patients, reported on the impact of pre-treatment sarcopenia in cancer patients.5 They found an overall pre-treatment prevalence of sarcopenia of 39%. Furthermore, they reported increased risk of death, higher rates of post-operative complications, and reduced tolerance to chemotherapy in the patients exhibiting sarcopenia.5 Sarcopenia has consistently been shown to be associated with dose-limiting toxicity (DLT)
across a wide variety of systemic anticancer treatments (single agents, combination treatments, cytotoxic chemotherapy, immunotherapy, and targeted agents) since 2007 with 41 studies to date supporting these findings. Furthermore, the relationship between sarcopenia and poor survival has been the topic of various systematic reviews and meta-analysis. In a recent systematic review of 35 studies that included 6894 patients with solid tumours, low muscle cross-sectional area was observed in 38.6% of patients before commencement of treatment was and associated with poorer overall survival, post-operative complications, and chemotherapy toxicity. While WL has been shown frequently to impair QoL, specifically with 10% WL being associated with significantly poorer QoL, overall and in each of the individual QoL domains (including physical functioning, role functioning, and social functioning). However, the link with sarcopenia is less well described. However, in a recent study of 237 advanced lung and gastrointestinal cancer patients, sarcopenia was associated with worse QoL, specifically higher rates of depression.

Little is known about the prevalence of CC or sarcopenia at national level. A systematic review by Anker et al. estimated the prevalence of CC to be 15.8/10 000 in Europe (2013) and 16.5/10 000 in the USA (2014). Another study by the same group estimated that 170 000 patients in Japan would experience CC annually (13.4/10 000). Other than these studies, the relative burden of the individual components of CC, namely, WL and sarcopenia, has not been well studied. The number of patients with cancer affected by sarcopenia and WL in Ireland and the UK is currently unknown. Given that approximately 338 499 people are diagnosed annually with cancer in the UK and Ireland, even modest proportions of patients affected by WL and sarcopenia could amount to a significant population at risk of negative clinical outcomes, which could be treated with intensive nutrition support. While little evidence exists on the ideal patient–dietitian ratio, the quantification of the current population in need of care may help identify the true number of patients who would benefit from individualized nutrition counselling or support, which may assist in the justification of increased dietetic staffing. Therefore, the aim of this study was to estimate the prevalence and annual incidence of cancer-related WL and sarcopenia in British and Irish populations.

Materials and methods

Annual incidence and prevalence of cancer: national registry data

The 2015 cancer annual incidence and prevalence data (by cancer site) for each country (Ireland, Northern Ireland, England, Scotland, and Wales) were obtained from publicly available data from the websites of their respective national cancer registries, while prevalence data for Northern Ireland were inclusive of 2017 and for Ireland included 2016. Prevalence data reported were limited to the date of opening of each cancer registry; therefore, the data presented do not account for diagnoses that pre-date registry records (prior to 1993–95).

Weight loss and sarcopenia: diagnostic criteria

Weight loss >5% in 6 months was chosen as the standard for this study as this is part of the diagnostic criteria for CC as per the international consensus definition. WL >10% in 6 months was also chosen as it constitutes clinically severe WL in general clinical populations. Sarcopenia assessed using computed tomography (CT) images at the level of the third lumbar vertebra are the gold standard measure of body composition assessment and is an additional diagnostic criterion in the international consensus definition. Thus, when recording the prevalence of sarcopenia from the literature, studies chosen for inclusion were limited to those that measured body composition using lumbar CT scans. This technique to assess skeletal muscle area involves manually outlining the skeletal muscle components and measuring the area of the tissue, which falls within the recognized thresholds for muscle based on Hounsfield unit (HU) (−29 to +150 HU). Skeletal muscle area is normalized for stature to compute the skeletal muscle index (SMI). Patients are classified as sarcopenic based on SMI cut-points and given the heterogeneity in the cut-points used to define sarcopenia in oncology patients; only studies that defined sarcopenia using one of the three most commonly used criteria were included as these have been widely validated. These definitions are as follows: Prado et al.: SMI <52.4 cm²/m² in men and <38.5 cm²/m² in women; Martin et al.: SMI <43.0 cm²/m² in men with a body mass index (BMI) <25 kg/m² and <53.0 cm²/m² in men with a BMI <25 kg/m² and BMI <41.0 cm²/m² in women; and Baumgartner et al. converted dual X-ray absorptiometry cut-points by Mourtzakis et al. as SMI <55.4 cm²/m² in men and <38.9 cm²/m² in women.

Weight loss and sarcopenia: literature review

A systematic review using PubMed was conducted to identify the reported prevalence of WL and sarcopenia across primary tumour locations. After screening initial results and confirming inclusion of known studies of relevance and further studies listed in the references of other systematic reviews, 179 papers were identified, which reported WL or sarcopenia in cancer patients. Studies were then excluded where they did not report

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a rate of WL over a 6 month period or CT-diagnosed sarcopenia. Furthermore, as site-specific cancer prevalence data were not available for all included regions, to limit impact of heterogeneity in included studies, studies that were only included early or metastatic disease was excluded from the final analysis. Finally, six studies were included where individual cancer groups were reported and both 5% and 10% WL were reported. These studies contributed 2340 patients cumulatively. In addition, six studies were retained, which included patients across all stages of disease (n = 2916) and assessed for sarcopenia using widely validated CT cut-points.

Details of the studies included in the final analysis are shown in Table 1. Figure 1 is a schematic of the progressive exclusion of studies according to the inclusion/exclusion criteria outlined as follows:

- **Inclusion criteria**
  - Studies describing point prevalence of 6 month WL > 5% or 10% in cancer patients
  - Studies describing point prevalence of CT-diagnosed sarcopenia in cancer patients using Prado et al.27 Martin et al.28 or Mourtzakis et al.29 cut-points

- **Exclusion criteria**
  - Non-English language
  - No full text
  - Non-human
  - Paediatric studies
  - Studies limited to specific disease stages

### Weight loss and sarcopenia: local Irish data

As the data in the literature for the prevalence of WL and sarcopenia were scarce, prevalence data were obtained from a local database from University College Cork, where over a 6 year period, body composition data were collected prospectively on 1015 ambulatory cancer patients across two designated cancer centres, and these data have formed part of a number of previously published studies (methods described elsewhere).31–35 All solid invasive cancers across all stages were eligible for inclusion in this study, including lymphomas but excluding head and neck cancers, which were not treated at these centres (see Table 2).

### Weight loss and sarcopenia: calculating annual incidence and prevalence

In order to account for heterogeneity, only studies that included patients at all stages of disease were included in these

| Author et al.37 | Country | Site | n | % with WL > 5% with WL > 10% | Author et al.37 | Country |
|----------------|---------|------|---|-----------------------------|----------------|---------|
| Correia et al.37 | Portugal | Gastric | 48 | 50.0 | Correia et al.37 | Portugal |
| Pacelli et al.38 | Italy | Gastric | 196 | 42.0 | Pacelli et al.38 | Italy |
| Pressoir et al.39 | France | Upper GI and HBP | 103 | 63.2 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Upper GI/HBP | 35 | 68.6 | Sanchez-Lara et al.40 | Mexico |
| Pressoir et al.39 | France | CRC | 156 | 47.5 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | CRC | 20 | 30.0 | Sanchez-Lara et al.40 | Mexico |
| Malietzis et al.41 | UK | CRC | 805 | 42.9 | Malietzis et al.41 | UK |
| Pressoir et al.39 | France | Head and neck | 156 | 42.9 | Pressoir et al.39 | France |
| Kabarriti et al.42 | USA | Head and neck | 158 | 42.9 | Kabarriti et al.42 | USA |
| Fattouh et al.43 | USA | Head and neck | 114 | 36.0 | Fattouh et al.43 | USA |
| Pressoir et al.39 | France | Leukaemia, lymphoma, and myeloma | 156 | 36.0 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Leukaemia, lymphoma, and myeloma | 25 | 36.0 | Sanchez-Lara et al.40 | Mexico |
| Zhang et al.44 | China | Lymphoma | 132 | 34.0 | Zhang et al.44 | China |
| Pressoir et al.39 | France | Ovary and uterus | 137 | 45.1 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Cervix/uterus/ovary | 12 | 66.7 | Sanchez-Lara et al.40 | Mexico |
| Pressoir et al.39 | France | Breast | 375 | 42.4 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Breast | 61 | 11.5 | Sanchez-Lara et al.40 | Mexico |
| Pressoir et al.39 | France | Lung | 90 | 49.4 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Lung | 11 | 45.5 | Sanchez-Lara et al.40 | Mexico |
| Pressoir et al.39 | France | Other | 349 | 36.7 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Other | 27 | 33.3 | Sanchez-Lara et al.40 | Mexico |
| Meza-Junco et al.45 | USA | Liver | 116 | 36.0 | Meza-Junco et al.45 | USA |
| Pressoir et al.39 | France | Mixed | 1545 | 40.9 | Pressoir et al.39 | France |
| Sanchez-Lara et al.40 | Mexico | Mixed | 191 | 35.6 | Sanchez-Lara et al.40 | Mexico |
| Mauricio et al.46 | Brazil | Mixed | 228 | 22.0 | Mauricio et al.46 | Brazil |
| Martin et al. (2013)28 | Canada | Mixed | 1473 | 22.0 | Martin et al. (2013)28 | Canada |
| Prado et al. (2008)27 | Canada | Mixed | 250 | 22.0 | Prado et al. (2008)27 | Canada |

CRC, colorectal cancer; GI, gastrointestinal; HBP, hepatobiliary/pancreatic; WL, weight loss.
Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram describing literature search for weight loss (WL) and sarcopenia prevalence in cancer.

![Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram](image)

Table 2 Rates of WL and sarcopenia in Irish cancer patients with solid tumours

| Site                | n  | ≥5% WL in 6 months | ≥10% WL in 6 months | n CT | Sarcopenic |
|---------------------|----|--------------------|---------------------|------|------------|
| Breast              | 94 | 13.80%             | 6.40%               | 80   | 42.50%     |
| CRC                 | 258| 31.80%             | 11.60%              | 264  | 37.10%     |
| GU                  | 54 | 27.80%             | 11.10%              | 48   | 41.70%     |
| Gynaecological      | 54 | 40.70%             | 22.20%              | 54   | 37.70%     |
| Haematological      | 93 | 29.00%             | 17.20%              | 95   | 37.90%     |
| HPB                 | 94 | 53.20%             | 27.70%              | 94   | 44.70%     |
| Lung                | 117| 26.50%             | 12.00%              | 119  | 38.70%     |
| Upper GI            | 147| 52.40%             | 29.00%              | 146  | 43.20%     |
| Other               | 49 | 34.70%             | 14.30%              | 39   | 33.30%     |
| Overall             | 960| 34.80%             | 16.60%              | 940  | 39.40%     |

CRC, colorectal cancer; CT, computed tomography; GI, gastrointestinal; GU, genitourinary; HBP, high blood pressure; WL, weight loss. Methods and demographics have been described previously.31
analyses. Data from the Irish study were used to supplement the data obtained from the literature. The reported prevalence of WL and sarcopenia according to cancer site was collated, and weighted means for each site and condition were calculated according to the formula $\bar{x} = \frac{\sum P_i n_i}{\sum n_i}$, where $P_i$ is the prevalence reported in each study and $n_i$ is the respective sample size.

The weighted means (see Table 3) were subsequently used to crudely extrapolate the estimated annual incidence and prevalence of these conditions, according to cancer site among cancer survivors across the UK and Ireland based on the national cancer registry data. Annual incidence was estimated for each individual cancer group using the formula $I_e = I \times M$, where $I_e$ is the site-specific estimated annual incidence of WL or sarcopenia related to cancer, $I$ is the annual incidence of cancer cases, and $M$ is the weighted mean of the reported point prevalence of WL or sarcopenia. The condition-specific $I_e$ for each cancer group was then summed to give an overall annual incidence for each condition. This represents the number of new cases of cancer-related WL or sarcopenia that would be likely to occur in any given year based on the number of cancer cases.

Prevalence was extrapolated for each individual cancer group using the formula $P_e = P \times M$, where $P_e$ is the estimated prevalence of WL or sarcopenia related to cancer, $P$ is the prevalence of cancer cases, and $M$ is the weighted mean of the reported point prevalence of WL or sarcopenia. The condition-specific $P_e$ for each cancer group was then summed to give an overall prevalence for each condition.

**Missing data**

While most cancer groups had WL and sarcopenia reported at least once in the literature or in the local database, data regarding melanoma were not available, and thus, these cases were combined into the ‘other’ group, which also included endocrinological, sarcoma, and central nervous system cancers. Therefore, WL and sarcopenia rates on a population level were extrapolated using site-specific data from the literature for 96% of cancer cases, and the remaining 4% were extrapolated based on data from studies on mixed cohorts.

**Results**

**Cancer annual incidence and prevalence**

Across the UK and Ireland, an average of 380 964 patients are diagnosed with cancer annually, and it is estimated that 2 308 785 patients are currently living with cancer across both regions. In Ireland, according to the National Cancer Registry of Ireland (NCRI), an average of 22 000 cases of invasive cancers (excluding non-melanoma skin cancer) were diagnosed annually between 2015 and 2017, which equates to an incidence rate of 478 (men) and 387 (women) cases per 100 000 per year. The most common cancers among men and women are prostate and breast cancer, respectively, followed by colorectal and lung cancer. Looking at cancer survivorship, a total of 156 469 cancer patients, diagnosed since January 1994, were still alive at the end of 2016 in Ireland.

**Cancer-related weight loss**

The reported prevalence of WL > 5% over 6 months in the literature ranged between 11.5% and 68.6% depending on primary site. The prevalence of WL > 10% over 6 months ranged from 5.0% to 54.3%. See Table 1 for site-specific rates, in patients at any stage of disease. Local data are shown in Table 2. Rates of WL and sarcopenia according to primary site reported in the scientific literature and also as seen in local data (including weighted means) are displayed in Table 3. Taking into account relative prevalence of the various cancer sites, it is estimated that 33.8% of cancer patients experience WL > 5% annually.

We estimate that across Ireland and the UK, at least 101 204 cancer patients (7251 Ireland) are affected by

| Site               | n weight | ≥5% WL in 6 months | ≥10% WL in 6 months | n CT | Sarcopenic |
|--------------------|----------|-------------------|---------------------|------|-----------|
| Upper GI           | 623      | 47.90%            | 30.30%              | 146  | 43.20%    |
| HBP                |          |                   |                     |      |           |
| Breast             | 530      | 20.90%            | 10.60%              | 210  | 36.60%    |
| Head and neck      | 179      | 56.60%            | 37.10%              | 272  | 66.30%    |
| CRC                | 434      | 37.40%            | 15.40%              | 1069 | 54.50%    |
| Haematological     | 406      | 25.30%            | 26.10%              | 95   | 37.90%    |
| Gynaecological     | 203      | 45.20%            | 26.70%              | 55   | 32.7%     |
| Lung               | 218      | 36.90%            | 20.00%              | 119  | 38.70%    |
| GU                 | 54       | 27.80%            | 11.10%              | 48   | 41.10%    |
| Other              | 425      | 36.30%            | 18.20%              | 39   | 33.30%    |
| Mixed              | 2696     | 38.40%            | 20.90%              | 2663 | 37.80%    |
| Overall            | 5996     | 37.30%            | 21.80%              | 4796 | 43.30%    |

CRC, colorectal cancer; CT, computed tomography; GI, gastrointestinal; GU, genitourinary; HBP, high blood pressure; WL, weight loss.
Table 4  Estimated annual incidence of cancer-related malnutrition (WL and sarcopenia) in Ireland and the UK calculated using weighted means of WL and sarcopenia prevalence as shown in Table 3 and cancer statistics from the national cancer registries

| Country          | England | Scotland | Wales | Northern Ireland | Ireland | Ireland and UK (total) |
|------------------|---------|----------|-------|------------------|---------|------------------------|
|                  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  |
| Colorectal       | 13 959 | 5748     | 20 342| 1469   | 605     | 2141  | 901    | 371    | 1312  | 445    | 183     | 648    | 1055   | 434     | 1537 |
| Upper GI         | 6280   | 3972     | 5664  | 731    | 462     | 659   | 429    | 271    | 378   | 194    | 122     | 175    | 485    | 307     | 437  |
| Respiratory      | 13 890 | 7528     | 14 567| 1833   | 994     | 1923  | 903    | 490    | 947   | 458    | 248     | 480    | 895    | 485     | 939  |
| Genitourinary    | 16 441 | 6565     | 4309  | 1334   | 533     | 385   | 1020   | 407    | 228   | 468    | 187     | 141    | 1192   | 476     | 257  |
| Hepatobiliary pancreatic | 7064 | 4469     | 5398  | 776    | 491     | 593   | 464    | 293    | 354   | 235    | 149     | 180    | 474    | 300     | 362  |
| Breast           | 9635   | 4887     | 19 593| 993    | 504     | 2020  | 593    | 301    | 1205  | 307    | 156     | 624    | 694    | 352     | 1411 |
| Gynaecological   | 7892   | 4662     | 5710  | 883    | 521     | 639   | 496    | 293    | 359   | 265    | 157     | 192    | 548    | 324     | 397  |
| Melanoma         | 4848   | 2431     | 4448  | 493    | 247     | 452   | 285    | 143    | 261   | 146    | 73      | 134    | 425    | 213     | 390  |
| Head and neck    | 5509   | 3611     | 6453  | 724    | 475     | 849   | 388    | 254    | 454   | 205    | 134     | 240    | 392    | 257     | 459  |
| Haematological   | 6798   | 7013     | 10 184| 600    | 619     | 899   | 431    | 445    | 646   | 196    | 202     | 294    | 434    | 448     | 650  |
| Other            | 8888   | 4456     | 8153  | 988    | 495     | 906   | 548    | 275    | 503   | 237    | 119     | 217    | 658    | 330     | 604  |
| Total (n)        | 101 204| 55 341   | 104 819| 10 825| 5946    | 11 465| 6457   | 3542   | 6657  | 3155   | 1730    | 3324   | 7251   | 3925    | 7442 |
| Patients affected| 33.70% | 18.40%   | 34.90%| 34.60% | 19.00%  | 36.70%| 34.00% | 18.60% | 35.00%| 34.10% | 18.70%  | 35.90% | 33.80% | 18.30%  | 34.70%|

GI, gastrointestinal; WL, weight loss.
Sarc refers to sarcopenia diagnosed using computed tomography at the level of third lumbar vertebra.

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Table 5  Estimated prevalence of cancer-related malnutrition (WL and sarcopenia) among cancer patients in Ireland and the UK calculated using weighted means of WL and sarcopenia prevalence as shown in Table 3 and cancer statistics from the national cancer registries

| Country                  | England | Scotland | Wales | Northern Ireland | Ireland | Ireland and UK (total) |
|--------------------------|---------|----------|-------|------------------|---------|------------------------|
|                          | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  | WL 5%  | WL 10%  | Sarc  |
| Colorectal               | 81 011 | 33 358  | 118 051 | 9636   | 3968    | 14 041 | 5238   | 2157    | 7633   | 3202   | 1318    | 4666  | 7061   | 2908    | 10 290 |
| Upper GI                 | 14 802 | 9363  | 13 350  | 1748   | 1106    | 1577   | 950    | 601     | 857    | 617    | 390     | 556   | 1536   | 972     | 1385   |
| Respiratory              | 21 946 | 11 895 | 23 017  | 3150   | 1707    | 3304   | 1376   | 746     | 1443   | 855    | 463     | 896   | 2060   | 1116    | 2160   |
| Genitourinary            | 121 252| 48 414 | 23 204  | 10 208 | 4076    | 2426   | 8113   | 3239    | 1488   | 3853   | 1539    | 889   | 11 887 | 4746    | 1853   |
| Hepatobiliary pancreatic| 6669   | 4218   | 5095    | 834    | 5 28    | 637    | 229    | 145     | 175    | 233    | 147     | 178   | 623    | 394     | 476    |
| Breast                   | 99 442 | 50 435 | 202 215 | 10 275 | 5211    | 20 894 | 5962   | 3024    | 12 124 | 3343   | 1695    | 6798  | 7405   | 3756    | 15 059 |
| Gynaecological           | 64 345 | 38 009 | 46 551  | 7460   | 4407    | 5397   | 3332   | 1968    | 2411   | 2604   | 1538    | 1884  | 5169   | 3053    | 82 910 |
| Melanoma                 | 43 922 | 22 021 | 40 292  | 4857   | 2435    | 4456   | 2478   | 1243    | 2273   | 1606   | 805     | 1474  | 3919   | 1965    | 3595   |
| Head and neck            | 33 723 | 22 105 | 39 503  | 4625   | 3031    | 5417   | 2347   | 1539    | 2749   | 1241   | 814     | 1454  | 1568   | 1028    | 1837   |
| Haematological           | 42 947 | 44 305 | 64 336  | 4294   | 4430    | 6432   | 1914   | 1974    | 2867   | 1550   | 1599    | 2323  | 3774   | 3894    | 5654   |
| Other                    | 23 889 | 11 978 | 21 915  | 2128   | 1067    | 1952   | 2633   | 1320    | 2415   | 871    | 437     | 799   | 3407   | 1708    | 3126   |
| Total (n)                | 553 950| 296 101 | 597 529 | 59 215 | 31 966  | 66 534 | 34 573 | 17 956  | 36 436 | 19 975 | 10 746  | 21 916| 48 410 | 25 540  | 49 174  |
| Patients affected        | 30.90% | 16.50% | 33.40%  | 31.80% | 17.10%  | 35.70% | 31.10% | 16.20%  | 32.80% | 31.50% | 16.90%  | 34.60%| 30.90% | 16.30%  | 31.40%  |

GI, gastrointestinal; WL, weight loss.
Sarc refers to sarcopenia diagnosed using computed tomography at the level of third lumbar vertebra.
WL > 5% annually and that there are 553 950 cancer survivors (48 410 Ireland) who have suffered >5% WL at some point in their disease trajectory. This degree of WL is diagnostic of CC according to the international consensus criteria. Of these, we estimate that 55 341 cancer patients (3925 Ireland) are affected by WL > 10% and that there are 296 101 cancer survivors (25 540 Ireland) who have suffered >10% WL. Tables 4 and 5 show the relative abundance of cases by cancer site and country. Taking into account relative prevalence of the various cancer sites, it is estimated that 18.5% of cancer patients experience WL > 10% annually. Given the mid-year populations reported for 2015, this corresponds to 18.48/10 000 in the population developing WL > 5% related to cancer each year, 10.11/10 000 of which would experience WL > 10%.\textsuperscript{15,36}

**Cancer-related sarcopenia**

The reported prevalence of sarcopenia in the literature ranged between 15.0% and 70.9% depending on the tumour type (Table 4). Local data are shown in Table 2.

Furthermore, we estimate that there are at least 104 819 annual cases (7442 Ireland) of sarcopenia among cancer patients in Ireland and the UK. We estimate that there are 597 529 cancer survivors alive (49 174 Ireland) who have been affected by sarcopenia during their disease trajectory. Tables 4 and 5 show the relative abundance of cases by cancer site and country. Taking into account relative prevalence of the various cancer sites, it is estimated that 35.1% of cancer patients experience sarcopenia annually. Given the mid-year populations reported for 2015, this corresponds to 19.17/10 000 in the population with both cancer and sarcopenia.\textsuperscript{15,36}

**Discussion**

To our knowledge, this is the first study reporting the epidemiology of cancer-related WL and sarcopenia, specifically. A systematic review by Anker et al. reported the corresponding estimates for CC, which is a syndrome encompassing WL and sarcopenia. They estimated the prevalence of CC to be 15.8/10 000 in Europe (2013) and 16.5/10 000 in the USA (2014).\textsuperscript{13} This is in the same order of magnitude as the present study, which estimated 18.5/10 000 for WL > 5% and 19.2/10 000 for sarcopenia in Ireland and the UK. Another study by the same group estimated that 170 000 patients in Japan would experience CC annually (13.4/10 000).\textsuperscript{14} While the figures in the present study are marginally higher than previously published estimates, this is partially explained by WL and sarcopenia often being co-morbid, and so the populations affected by each condition are not mutually exclusive.\textsuperscript{47} The high incidence of WL and sarcopenia in these populations is clinically relevant because of their association with poor outcomes in cancer patients.\textsuperscript{38,48,49}

A recent review on the toxicity of cancer treatments in sarcopenia by Hilmi et al. reported that of 32 studies evaluating chemotoxicity, 24 studies found a significant increase in sarcopenic patients. Similarly, they found that seven of eight studies in targeted therapies demonstrated the same increased risk of toxicity in sarcopenia, and finally, they assessed immunotherapy studies that were less numerous, but three of four studies found an increased rate of toxicities among those with sarcopenia.\textsuperscript{50} Previously published reports by our group have shown that patients being treated for renal cell carcinoma with sunitinib who suffer DLT within 6 months of starting therapy had significantly lower SMI. Interestingly, while the mean SMI of those suffering early DLT was lower, it did not reach the cut-point for sarcopenia. This suggests a dose–response relationship with an advantage of higher muscle mass, outside the range of frank sarcopenia (52 vs. 59 cm²/m², \(P = 0.01\)).\textsuperscript{33}

A recent systematic review incorporating 35 studies (6894 patients) found that 8 of 11 studies that evaluated pre-operative sarcopenia showed significant independent associations between pre-treatment sarcopenia and serious post-operative complications after gastrectomy, pancreatectomy, oesophagectomy, and hepatic resections.\textsuperscript{5} A further two of these studies found an independent increased risk of hospital acquired infections post-colectomy in patients with pre-treatment sarcopenia.\textsuperscript{5}

Both WL and sarcopenia have been associated with increased mortality in cancer. In a large US study of 4258 patients with cancers across all major primary sites (15% metastatic), WL > 10% at diagnosis was associated with increased risk of death vs. weight stability [hazard ratio: 2.5; 95% confidence interval (CI): 1.3–4.8, \(P < 0.001\)].\textsuperscript{51} A study across Canada and the European Union of 8160 patients showed similarly increased risk in patients suffering WL, at all BMI classes.\textsuperscript{52} Pamoukdjian et al.\textsuperscript{5} performed a meta-analysis of 22 studies with 5351 participants to examine the association between pre-treatment sarcopenia and post-operative survival. This group reported that 13 studies showed an independent association between pre-treatment sarcopenia and post-operative survival, 5 with peri-chemotherapy survival, 3 with post-operative relapse-free survival, and 2 with post-chemotherapy progression-free survival.\textsuperscript{5} Shachar et al. reviewed 7779 patients across 37 studies in a meta-analysis in 2016, of which 22 has multi-variate analyses available. Using only those studies that reported a multivariate model, they found a summary hazard ratio of 1.5 (95% CI: 1.4–1.7, \(P < 0.001\)) for overall survival suggesting a significantly increased risk of death in cancer patients who have sarcopenia.\textsuperscript{7}

Quality of life is also impacted in patients with WL and sarcopenia. Numerous studies have demonstrated poorer QoL using a variety of validated tools in patients experiencing...
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WL due to cancer.\textsuperscript{10,11,53,54} A systematic review of health-related QoL (HRQoL) instruments in 2013 found that 23 of 27 studies that examined HRQoL in relation to WL found a significant detriment to HRQoL in those who experienced greater WL, although the definitions of WL differed widely and the tools used to assess HRQoL varied also.\textsuperscript{10} In haematological cancer patients surveyed with the SF-36 HRQoL tool before stem cell transplantation, bodily pain, vitality, and physical function scores were poorer in those with sarcopenia.\textsuperscript{55} While one study of breast cancer patients did not find a significant difference between patients based on sarcopenia, the sample size was small.\textsuperscript{56} Recently, our group has shown that WL was an independent predictor of poorer global QoL in the setting of advanced cancer (n = 1027) [WL > 5% odds ratio (OR): 1.6, P = 0.048; WL > 10% OR: 2.7, P < 0.001]; however, sarcopenia was only associated with physical function score on univariate analysis [OR 1.7 (95% CI: 1.3–2.3), P < 0.001].\textsuperscript{54}

The estimations provided by this study indicate that a large population exists who may be at greater risk of frailty as they enter old age with reduced reserves. Of note, hospitalizations (42% vs. 11%, P < 0.001), falls (18% vs. 55%, P < 0.001), and fear of falls (12% vs. 57%, P < 0.001) were more prevalent in the frail in a representative sample of US older adults.\textsuperscript{57} Fear of falls is likely to impact activity levels and lead to further deconditioning.\textsuperscript{58} While the systematic review by Pamoukdjian \textit{et al.}\textsuperscript{5} failed to identify any studies evaluating the risk of disability in relation to pre-treatment sarcopenia, Prado \textit{et al.}\textsuperscript{27} found that sarcopenia was associated with poor functional status in the sarcopenic patients of their lung and gastrointestinal cancer cohort. Similarly, a recent study of an elderly mixed cancer cohort has demonstrated that patients with cachexia experience significant impairments in their instrumental activities of daily living.\textsuperscript{47} Importantly, hospitalizations are associated with worsening of weight status.\textsuperscript{59} This is particularly concerning as the Irish and British populations are aging and the burden of frailty will increase alongside this population trend.\textsuperscript{60,61}

In addition to patient-centred outcomes, the economic impact of cancer-related malnutrition is important to consider. The British Association for Parenteral and Enteral Nutrition commissioned a report in 2015, which reported that malnourished patients cost the National Health Service more annually than those who were not at risk of malnutrition (\textsterling}7408/\textsterling}8408 vs. \textsterling}2155/\textsterling}2445).\textsuperscript{3} An Irish study that replicated the British Association for Parenteral and Enteral Nutrition methodology found that at least \textsterling}750 million annually in additional healthcare costs were accrued in the care of malnourished patients in Ireland, equating to approximately \textsterling}357 extra per patient affected by disease-related malnutrition.\textsuperscript{4}

This study has a number of limitations that must be acknowledged. Firstly, the data available in the literature documenting WL according to the standard 5% and 10% over 6 months and sarcopenia using third lumbar vertebra CT images are limited. Many articles that were identified during the literature search could not be included as they reported mean WL, proportions of patients with any WL or with sarcopenia measured using non-standard techniques. Secondly, while the incidence rates reported herein are likely to be good estimates based on the available data, caution must be applied in the interpretation of the prevalence data. There is an inherent survival bias because WL and sarcopenia are associated with increased risk of death in cancer. Thus, those suffering from WL or sarcopenia would have greater risk of death, and therefore, their transfer from incident to prevalent cases would not be a 1:1 with unaffected patients. Furthermore, to our knowledge, there is no evidence to suggest how many of these cases would resolve after treatment of the underlying cancer. Thus, the prevalence data we present herein represent the number of cancer survivors who are likely to have suffered WL or sarcopenia due to their cancer at some time in the past but does not accurately represent the point prevalence of these conditions and, consequently, is likely an overestimate. Despite these limitations, the study has notable strengths. This is the first study of its kind estimating the burden of WL and sarcopenia related to cancer in the British Isles. A thorough literature search was conducted, and a large local database was used to complement gaps in the literature. In addition, specific parameters were chosen for WL and sarcopenia, which were clinically relevant and in accordance with the international consensus definition. In order to provide more accurate estimates of the burden of cancer-related malnutrition, future studies should report these using standardized, clinically relevant measures.

Conclusion

In conclusion, this is the first report estimating the burden of cancer-related WL and sarcopenia across the UK and Ireland. These figures are crude estimates that are limited by gaps in the literature and potential survival bias. Ensuring that patients receive intervention for these changes in body composition is of the utmost importance, in order to optimize outcomes for patients undergoing palliative treatments and to aid recovery towards pre-diagnosis baseline in patients expected to achieve a cure and enter long-term survivorship. Given the impact of malnutrition on cancer outcomes during treatment and the long-term impact of sarcopenia on frailty among survivors, urgent attention is required to address gaps in access to nutrition care available to cancer patients.

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**Conflict of interest**

None declared.

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**Ethical approval and consent to participate**

Ethical approval was granted for the human data collected by Clinical Research Committee of the Cork Teaching Hospitals [ECM 4 (g) 03/03/15], and informed consent was obtained for all human subjects. The study was conducted in accordance with the Declaration of Helsinki.

**Consent for publication**

N/A.

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**Data availability**

Results of local study are archived in accordance with GDPR. National cancer registry data were obtained from as follows:

- [http://www.ukiacr.org/kpis](http://www.ukiacr.org/kpis)
- [http://www.ncin.org.uk/about_ncin/segmentation](http://www.ncin.org.uk/about_ncin/segmentation)
- [https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/All-Types-of-Cancer/](https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/All-Types-of-Cancer/)
- [https://public.tableau.com/views/](https://public.tableau.com/views/)
- CancerincidencenumberofnewcasesandprevalencepeoplelivingafterdiagnosisofcancerforclusternetworksinWales/Introduction?embed=y&showVizHome=no
- [http://www.qub.ac.uk/research-centres/ncir/CancerInformation/official-statistics/BySite/](http://www.qub.ac.uk/research-centres/ncir/CancerInformation/official-statistics/BySite/)
- [https://www.nci.ie/sites/ncri/files/pubs/annualreport2018_26112018.pdf](https://www.nci.ie/sites/ncri/files/pubs/annualreport2018_26112018.pdf)

**Authorship**

E.S.S. conducted the literature review and extrapolations and drafted the manuscript; L.E.D. conducted the literature review and data collection on local data presented; D.G.P. helped write the manuscript; and A.M.R. conceived the study and helped write the manuscript. All authors reviewed the final manuscript.
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