

review

# Socioeconomic inequalities in cancer incidence in Europe: a comprehensive review of population-based epidemiological studies

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**Background.** Since the end of the previous century, there has not been a comprehensive review of European studies on socioeconomic inequality in cancer incidence. In view of recent advances in data source linkage and analytical methods, we aimed to update the knowledge base on associations between location-specific cancer incidence and individual or area-level measures of socio-economic status (SES) among European adults.

**Materials and methods.** We systematically searched three databases (*PubMed*, *Scopus* and *Web of Science*) for articles on cancer incidence and SES. Qualitative synthesis was performed on the 91 included English language studies, published between 2000 and 2019 in Europe, which focused on adults, relied on cancer registry data and reported on relative risk (RR) estimates.

**Results.** Adults with low SES have increased risk of head and neck, oesophagogastric, liver and gallbladder, pancreatic, lung, kidney, bladder, penile and cervical cancers (highest RRs for lung, head and neck, stomach and cervix). Conversely, high SES is linked with increased risk of thyroid, breast, prostate and skin cancers. Central nervous system and haematological cancers are not associated with SES. The positive gap in testicular cancer has narrowed, while colorectal cancer shows a varying pattern in different countries. Negative associations are generally stronger for men compared to women.

**Conclusions.** In Europe, cancers in almost all common locations are associated with SES and the inequalities can be explained to a varying degree by known life-style related factors, most notably smoking. Independent effects of many individual and area SES measures which capture different aspects of SES can also be observed.

Key words: socioeconomic status; socioeconomic inequality; cancer incidence; adults; Europe; cancer registry; relative risk

## Introduction

Health and disease are not distributed equally and often also not equitably. This has been observed since ancient times by prominent historical figures, such as Hippocrates (or else his contemporaries), who pointed out that higher social standing (power, wealth, freedom, etc.) was reflected in better health<sup>1</sup>, German physician Johann Peter Frank, a pioneer in public health who held the view that misery of the common people was the mother of disease<sup>2</sup>, and Louis René Villermé, who in 19<sup>th</sup> cen-

tury France combined census and mortality data and used this innovative way to show that disease distribution and life expectancy were associated with the distribution of poverty in terms of occupational class<sup>3,4</sup>, to name but a few.

When it comes to cancer, some of the earliest studies investigating social inequalities in Europe date back over a century. It was firmly established by then that certain occupations were undoubtedly associated with the development of malignancies – lung cancer in miners and scrotal cancer in chimney sweeps being the most notorious – but links

between social class and cancer were only starting to be explored. There were already observations that social classes differ with respect to cancer rates and mortality. According to some early researches, cancer on the whole was considered a disease of affluence<sup>5</sup>, while others found the opposite<sup>6,7</sup>, with differences probably being the result of unrefined, developing methodology. Later, when specific cancer types, most commonly gynaecological cancers in women, were investigated, clear differences were seen between classes, such that cervical and uterine cancers were found more frequently among poor while breast cancer was more common among wealthy women.<sup>8</sup>

A century or so after the first studies, in 1997 the International Agency for Research on Cancer (IARC) gathered available evidence from numerous epidemiological studies on the association between socioeconomic status (SES) and cancer morbidity and mortality which were considered to stem from associations between SES and cancer risk factors.<sup>2</sup> A 2019 IARC report responded to the knowledge gap for medium and low-income countries and addressed the importance of political will and know-how to reduce inequalities that are consistently found throughout the world.<sup>9</sup> Since the original IARC report, to our knowledge no

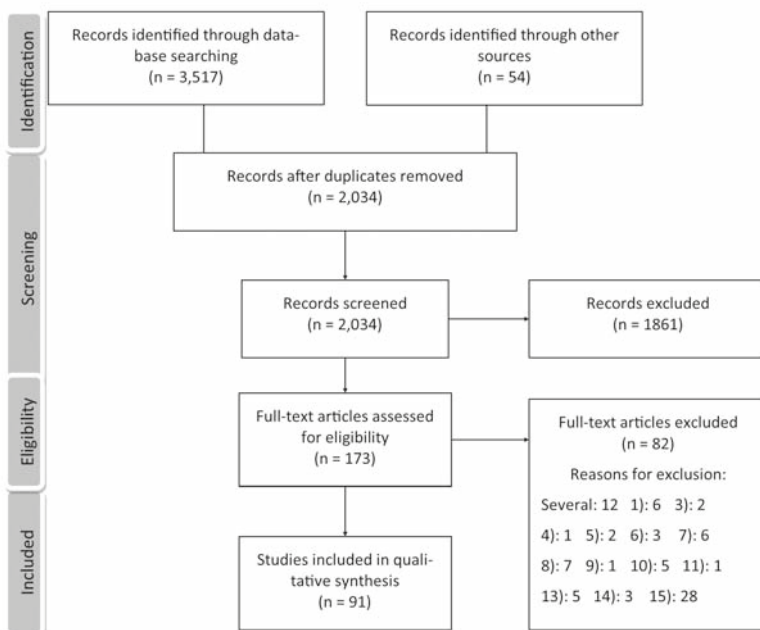
detailed review of cancer incidence in adults and SES in Europe has been published. In the intervening time, many new approaches for investigating inequalities have been developed, notably linkage methods that are increasingly used to combine data from many different databases with complete and accurate information on important socioeconomic variables, such as education, occupation and income. At the same time, methods have evolved which use area-based deprivation indices in determining how neighbourhoods influence the risk of cancer among their residents.<sup>9</sup> Finally, cancer inequalities should be viewed as dynamic instead of static, because the magnitude and direction of disparities can change in tandem with socially driven changes in determinants of health and disease.<sup>4</sup>

The aim of our work was thus to comprehensively review studies that have assessed the direction and magnitude of socioeconomic inequalities in location-specific cancer incidence among European adults in the 21<sup>st</sup> century. We specifically focused on studies that utilised population-based cancer registry data linked to individual or area-level measures of SES. As a result, a large burden of disease that could potentially be attributed to differences in SES in Europe is highlighted.

## Methodology

### Search strategy and inclusion/exclusion criteria

Pursuant to the main aim of our work and following the PRISMA guidelines<sup>10</sup>, in July 2019 we systematically searched three databases (*PubMed*, *Scopus* and *Web of Science*) for articles investigating the relationship between cancer incidence in adults in Europe and SES, operationalised either on an individual or area level, that relied (at least in part) on cancer registry/database data. The search strategy was thus constructed by combining six different main search terms with the Boolean operator 'AND' while using 'OR' for individual terms' synonyms. The computer-assisted searches were designed and performed by a research librarian. The main terms were: cancer, incidence, socioeconomic status, cancer registry, adults and Europe (for the full search strategy, refer to Supplementary table 1). European countries were defined according to the United Nations' definition of world regions, while any country that was a member of the European Network of Cancer Registries (ENCR) was additionally included. We searched in titles and abstracts of English-language articles pub-



**FIGURE 1.** The PRISMA diagram detailing the study selection process and results. Reasons for exclusion of full-text articles are indicated by numbers as they feature and are explained in the text under the subheading Search strategy and inclusion/exclusion criteria.

lished between 2000 and 2019. The search was updated in December 2019.

The PRISMA diagram detailing the study selection process and results is presented in Figure 1. First, duplicates were removed. After that two authors (AM and ST) independently selected articles for further reading based on their title and abstracts. Exclusion criteria at this stage (Screening in Figure 1) were: (1) the article was a review or a meta-analysis that included already identified studies; (2) the abstract did not include a description of methods used to assess the relationship between any SES measure (e.g. education, income, occupational social class, housing or other material determinant of SES, area deprivation) and incidence of any cancer, or did not at least mention that one of the goals/results was assessment of this relationship; (3) the study investigated exclusively all cancers combined; (4) the study population did not include adults; (5) the focus was comparison of two or more larger regions/countries; (6) the focus was on comparing rural and urban regions or else analysis by population density; (7) the study assessed primarily occupational risk or exposure through stratifying participants by type of occupation only (and not by occupational class); (8) the focus was on comparing immigrants and native-born or by ethnicity; (9) the study exclusively analysed incidence by marital status or cohabitation; (10) the study focused on SES-specific risk of advanced disease or primarily on the influence of screening (i.e. analysis of inequalities in detection rather than incidence of cancer was the main research goal); (11) the data on cancer was evidently not from a European country; (12) secondary (and not primary) cancers were analysed; (13) exploration of methodological issues was the main goal; (14) the study did not at all rely on data from cancer registries/databases.

If at least one author considered an article should be read in full, it was included in the list for full-text reading. In the next stage, two authors independently read each article in full to assess whether it should be included in the final selection. If there was uncertainty, a third author's opinion (VZ) was sought. Read articles were screened again using the above criteria, while a further exclusion requirement was also assessed (Eligibility in Figure 1). Namely, (15) if studies did not report results in terms of relative risk (RR) estimate between groups of SES, either as risk ratio, incidence rate ratio, odds ratio, age-standardised incidence rate ratio, standardised incidence ratio, relative index of inequality, standardised rate ratio, hazard ratio

or similar. In addition, a snowball approach was used whereby reference lists of articles that were read in full were searched manually for eligible records and conversely, articles that referenced the studies included in the final selection were manually examined. Several English-language cancer registry/database websites were also searched for relevant literature (reported under Identification in Figure 1).

## Study data extraction and results synthesis

After the articles for final inclusion were selected, we extracted from studies the following data: first author's full last name and first name initials; article title; studied country/-ies; journal (if available); publication year; study type, period and population; investigated cancer(s) with ICD or ICD-O codes (if available); SES indicator (and its level – individual/area); analysis methods and inequality measures; adjustment/stratification factors; possible study limitations; and main research findings.

Descriptive methods were used to report on the synthesis of research results regarding associations between different measures of SES and many different cancers in Europe. To examine more closely the gap between highest and lowest SES, we compiled cancer location-specific tables with RR estimates for the lowest compared to highest SES category. RR estimates were, when necessary, transformed so that highest SES was always the reference group, except in instances where SIR was calculated with reference to the whole population. The extracted information is provided comprehensively in the Supplementary tables 2–29, stratified by cancer site and by the type of the SES measure applied (individual or area-level).

## Results and discussion

### Lung cancer

Globally, lung cancer remains the most common cancer in absolute number of new cases<sup>11</sup> and 3<sup>rd</sup> in Europe where estimated age-standardised rates in men are roughly twice as high compared to women.<sup>12</sup> Smoking is the most important contributing cause of lung cancer and smoking rates vary significantly by SES. A vast amount of information on lung cancer and SES is available from across Europe that overwhelmingly points to increased risk with lower affluence, especially in men.<sup>13–35</sup> With respect to individual level SES (Supplementary table

2), lowest education was associated with a more than threefold risk in certain studies (RR for men and women generally around 1.8 and 1.5, respectively).<sup>13,14,23-25,31-33,36</sup> Very few studies have failed to confirm an increased risk, and only for women.<sup>29,30</sup> Occupational social class, the second most studied indicator of SES, is also a more prominent factor for men.<sup>13,29,35</sup> Comparatively few studies have attempted to evaluate the effect of material components of SES through income, housing tenure or characteristics and car ownership with similar or only slightly greater RR estimates in men compared to women.<sup>13,15,29</sup> Studies relying on area-level SES as a proxy for individual SES (Supplementary table 3) provided RR estimates in the same range.<sup>16-22</sup> Different individual and area factors when mutually adjusted or unadjusted exhibit comparable strength of association. Aside from unemployment, for which observed RRs were occasionally found to exceed 4<sup>13</sup> (a finding which could result also from reverse causality or significant comorbidity that was not adjusted for), generally, point estimates do not exceed RR of 2. Smoking inequality contributes most to lung cancer inequality, as confirmed by studies adjusting for smoking where it accounted for roughly 40–70% of the increased risk in low SES, whereas other lifestyle factors contribute much less.<sup>23,26,33</sup>

### Cancers of the upper aerodigestive tract and stomach cancer

Many European studies have shown cancers of the upper aerodigestive tract (UADT) to be strongly associated with lower SES (Supplementary tables 4 and 5).<sup>15-19,27,29,30,32,36-44</sup> As with lung cancer, the association is much stronger for men than women. In Italian<sup>29,30</sup>, Lithuanian<sup>32</sup> and multi-country European<sup>42</sup> studies for example, excess incidence of UADT and head and neck cancers among the lowest educated could only be confirmed for men. Similarly, in Germany, area deprivation was associated with elevated risk for oral cavity and upper respiratory tract cancers in men only.<sup>19</sup> The most studied individual-level SES indicator is education, for which overall RR estimates in men range from 1.5 to 3 and are generally even higher than those found for lung cancer. Effect of area deprivation in men in France<sup>16,17,37</sup>, Germany<sup>18,19</sup>, Spain<sup>38</sup> and Italy<sup>29</sup> was found to be between 1.5 and 2.0, whereas in a Scottish study cancers of the mouth, oropharynx and larynx were each shown to be twice to over 3-times as likely in people from the most deprived compared to the least deprived ar-

reas, though they did not stratify by sex.<sup>39</sup> There is convincing evidence that area deprivation has an independent effect on UADT cancer risk, not explained by individual factors.

Research on oesophageal and stomach cancers and SES also points to higher risks with lower individual (Supplementary table 6) and area (Supplementary table 7) SES.<sup>16,17,19,27,32,36,45-47</sup> Yet again, incidence in women seems to be less influenced by SES than in men. In several European countries, men of the lowest social standing or from the most deprived regions had between 1.3 to 3.0-times the risk of developing cancer of the oesophagus, whereas many studies found either less increased<sup>45,46</sup> or could not confirm an increased risk<sup>17,19,32,47</sup> for women, though even in the latter case the effect estimates were always positive, often with a discernible trend across SES categories. Given that different risk factors have been identified for the two major histological types, adenocarcinoma and squamous cell carcinoma (SCC), invaluable information comes from studies that investigated these subtypes and attempted to control for known risk factors in order to clarify to what extent they contribute to inequality. A nationwide case-control study in Sweden<sup>48</sup> found that fruit and vegetable intake as well as *Helicobacter pylori* infection (a potentially protective factor for oesophageal adenocarcinoma) could not explain any of the SES inequality for either histological subtype. Adjusting for reflux symptoms, body mass index (BMI) and tobacco in adenocarcinoma could explain only part of the SES inequality, whereas tobacco and alcohol in SCC did not contribute to SES inequality. Similarly, in a European multi-centre study<sup>49</sup> smoking, alcohol, BMI, physical activity and dietary intake of total energy as well as fruit, vegetable and meat consumption did not seem to contribute significantly to observed SES inequality in the incidence of oesophageal adenocarcinoma. Therefore, better designed approaches to measure these risk factors with minimised residual confounding as well as further research into as yet unidentified risk/protective factors are needed, especially given significant observed increases in incidence rates of oesophageal adenocarcinoma.<sup>50,51</sup>

Stomach cardia adenocarcinoma has been associated with the same risk factors as oesophageal adenocarcinoma and has also been observed to be on the rise.<sup>52</sup> On the other hand, occurrence of non-cardia adenocarcinoma which is linked to infection with *Helicobacter pylori*, has been declining.<sup>53</sup> Recent European registry-based studies that looked at the incidence of stomach cancer as

a whole found about 1.5-times (range from 1.1 to about 2) increased risk in lower SES individuals, predominantly men.<sup>16,19,29-32,45,54,55</sup> Rarely, no association could be confirmed for either sex.<sup>17,25,29</sup> There seem to be no major differences in terms of which SES indicator is used, though an Italian study, after adjusting for individuals' education, occupational class and housing characteristics, found no additional effect of area deprivation.<sup>29</sup> A meta-analysis of 11 European case-control and cohort studies estimated that the relative index of educational inequality (which takes into account the trend over categories and category sizes) for stomach cancer was as high as 2.92 (95% CI: 1.37-6.19).<sup>56</sup> When stomach cardia and non-cardia are analysed separately, conflicting conclusions are seen: sometimes associations of similar magnitudes are found for both subsites<sup>46</sup>; are somewhat stronger for non-cardia<sup>47</sup>; or somewhat stronger for cardia.<sup>49,57</sup> The two latter studies were large multi-centric case-control studies that also stratified by histological subtype and found more pronounced educational effects for intestinal compared to diffuse type of gastric adenocarcinoma. Furthermore, they investigated to what extent major risk factors explain SES inequality and both found that surprisingly little of the inequality could be attributed to lifestyle factors such as smoking, alcohol, diet, BMI and physical inactivity, or *Helicobacter pylori* infection.

### Liver, gallbladder and pancreatic cancers

Liver and gallbladder cancers are relatively rare in Europe, while the opposite is the case for pancreatic cancer. All come with a high mortality burden.<sup>58</sup> Relative risks for these three cancers of digestive organs comparing lowest to highest individual and area-level SES are listed in Supplementary tables 8 and 9.

High area-deprivation and low education are linked with up to twofold (usually around 1.5) increased risk of liver and gallbladder cancer.<sup>16,17,19,29,30,36,46,59-61</sup> Considering that many of the causes for these cancers are modifiable (chronic hepatitis B and C infection, alcohol, smoking, non-alcoholic fatty liver disease, obesity and gallstones<sup>62-64</sup>), they are very likely responsible for part of the observed SES inequality, though we can only speculate to what extent since we could not find studies adjusting for these factors.

Smoking, *Helicobacter pylori* infection and obesity could potentially explain up to half of all incident cases of pancreatic adenocarcinoma, the most

prevalent form of this cancer<sup>65</sup>, though our review did not reveal a uniform link with SES. On the one hand, low individual SES in Slovenia<sup>27</sup>, Denmark<sup>45</sup> and Sweden<sup>36</sup> and area deprivation in the United Kingdom (UK)<sup>59</sup> were linked to increased risk (RRs between 1.1-1.6). In Lithuania<sup>32</sup>, Germany<sup>19</sup> and Finland<sup>46</sup>, only men with lowest SES had a slightly increased risk. On the other hand, no effects could be seen in France<sup>16,17</sup> or Italy<sup>30</sup> and women in Lithuania with the lowest education actually had a reduced risk (RR 0.92).<sup>32</sup> Within the EPIC cohort, at first no significant effect was seen, although after the results were updated, RR estimates were further from unity and a higher risk in men with primary education or less was found. Confounding by known risk factors was also examined—risk was partly (in men) to almost fully (in women) accounted for by smoking, obesity, diabetes and physical inactivity.<sup>66,67</sup>

### Gynaecological and breast cancers

We found that low SES strongly increases the risk of invasive cervical cancer (Supplementary tables 10 and 11). RR estimates found in Europe vary between about 1.2 to 2.5 for the lowest compared to highest educated women.<sup>25,29-33,44,68-70</sup> When area deprivation is used, effect sizes are generally similar and also independent of individual SES.<sup>16-19,21,29,70-72</sup> Particularly prominent seem to be the effects of neighbourhood deprivation<sup>29,70</sup> and individual level material dimension of SES (e.g. income) which seemingly influence risk even more than education.<sup>29,44,68</sup> No contemporary studies investigating *in situ* carcinoma were found, though previously risk for *in situ* carcinoma was also higher with lower SES.<sup>73</sup> Very few authors adjusted for known risk factors, namely those relating to *Human papilloma virus* (HPV) infection, which is necessary for occurrence of cervical cancer, and smoking, which could hasten transformation of precancerous lesions into carcinoma.<sup>74,75</sup> In England, area effect was diminished when teenage conception rates, smoking rates and screening coverage were taken into account.<sup>76</sup> Similarly, in Norway, higher risk among the lower educated was not significant anymore, after controlling for smoking, age at first birth and participation in screening, though the hazard ratio was still close to 2.<sup>33</sup> Importantly, smoking accounted for more than 30% of the inequality, whereas screening and age at first birth contributed only approximately 3 and 6%, respectively. HPV seropositivity might explain the rest of the inequality, but as far as we know, neither this nor any other

study in Europe to date was able to make use of such data. Different histological subtypes have also rarely been studied separately—even though both squamous cell carcinoma and adenocarcinoma require HPV infection to develop, in Finland adenocarcinoma did not show an association with SES which could imply aetiology of the two subtypes varies to a larger degree than previously thought.<sup>69</sup> Cancers of the vulva and vagina are also associated with HPV infection, thus unsurprisingly, a negative association with SES has been observed with RR estimates as high as 2.<sup>44,59</sup>

Some of the highest rates of breast cancer incidence and mortality in the world are found in Europe where in places cumulative life-time risk for women is as high as 30%.<sup>58</sup> Unhealthy lifestyle, hormonal and reproductive factors (menarche, menopause, parity, age at first birth and breastfeeding) increase its risk.<sup>77-80</sup> As shown in Supplementary table 12, most studies found women with higher SES are at an increased risk of developing breast cancer.<sup>14,16,18,19,21,22,26-33,36,81-89</sup> Age-only adjusted RR estimates comparing lowest to highest education are between 0.6 and 0.9, mostly around 0.8. Similar estimates are reported when measuring area-SES (Supplementary table 13). Other measures of SES are used rarely and there seem to be less consistency between them, particularly in those that reflect material SES. Therefore, education through delay in childbearing seemingly explains most of the SES effect.<sup>90,91</sup> Studies that attempted to adjust also for reproductive and life-style factors found RRs either significantly closer to unity, when adjustment was incomplete<sup>82,85,87</sup>, or equal risk across SES categories both in pre- and postmenopausal women when adjustment was very careful.<sup>33,83,84,92</sup> Furthermore, no significant educational differences were found among nulliparous women.<sup>92</sup> Inequalities are also stronger for *in situ* compared to invasive breast cancer and remain partially unexplained by known risk factors<sup>30,87,92</sup> strongly suggesting the effect of screening. Overall, inequalities in breast cancer can thus, to a substantial degree, be explained by known risk factors.

Ovarian, fallopian tube and endometrial cancers have rarely been found to be positively associated with SES, most often no association was clearly determinable (Supplementary tables 10 and 11).<sup>16-19,30,32,36,68,93,94</sup> This is unexpected since reproductive/hormonal factors also play a role in tumorigenesis.<sup>95,96</sup> Equally rarely, increased risk of uterine<sup>97,98</sup> and ovarian<sup>36</sup> cancer among low SES groups has also been reported. No strong conclusion could be drawn for these cancers.

## Male genital and prostate cancers

Testicular cancer afflicts mostly adolescents and young men.<sup>99</sup> While it was previously thought that most of the risk for its development is determined already *in utero*, it is now evident that postnatal factors also play an important role, perhaps by influencing progression of existing *in situ* testicular carcinomas.<sup>100</sup> Across the world, increased risk of testicular cancer, which is predominantly of germ cell type classified into seminoma and non-seminoma, had often been reported with high SES but the gap has started to narrow in recent decades.<sup>101</sup> Since 2000 in Europe, many countries do not report an association (Supplementary tables 14 and 15); no difference in incidence was thus found in Denmark<sup>102</sup>, Slovenia<sup>27</sup>, Germany<sup>19,103</sup>, France<sup>16,17</sup> or Italy.<sup>30</sup> On the other hand, high area deprivation and household overcrowding in England<sup>59,104,105</sup>, low education in Sweden<sup>36</sup> and low occupational social class in Finland<sup>106</sup> were associated with lower risk of seminoma and non-seminoma cancer (RR estimates about 0.7-0.9), though in Finland, the RRs have decreased substantially. In line with findings that HPV infection, poor hygiene, smoking and obesity increase risk for penile cancer<sup>107</sup>, we found that most<sup>44,59,108</sup>, though not all<sup>106</sup>, identified studies also reveal an association between penile cancer and low SES, sometimes stronger for invasive than *in situ* carcinoma.

Representing over 20% of all incident cancer cases (excluding non-melanoma skin cancer), prostate cancer is the most common cancer among European men today.<sup>12</sup> The latest data shows that in most of Europe, incidence rates have stabilised or started decreasing.<sup>109</sup> Some of the potential lifestyle-related factors are smoking, alcohol, obesity, physical inactivity and diet, though no associations have been unequivocally proven.<sup>110,111</sup> However, today it is clear that the burden and its trend is highly influenced by availability of opportunistic screening for prostate cancer by Prostate Specific Antigen (PSA) testing. As shown in many studies (Supplementary tables 16 and 17), lower SES is associated with lower prostate cancer risk, though not everywhere.<sup>19,26,28,112</sup> RRs are between approx. 0.5–0.9, most often around 0.8, again with independent effects of different SES indicators.<sup>14,16-18,22,25,27,29-32,36,71,102,106,113-116</sup> Higher RRs are reported for less compared to more advanced disease<sup>106,113,115</sup>; this points to screening as one of the reasons for the positive gap (affluent men have better access to or are more motivated to undergo opportunistic screening). The gap was increasing

during the first decade of the 21<sup>st</sup> century<sup>59,115</sup>, but has since decreased in certain places<sup>22</sup>, perhaps due to changes in clinical use of PSA testing after negative outcomes related to opportunistic screening were becoming increasingly recognised. In a randomised intervention study<sup>113</sup>, screening somewhat narrowed the gap for advanced disease when education and income were used as measures of SES, while the gap for renters compared to homeowners widened. Finally, a cohort study in the UK found that adjustment for PSA testing narrowed the gap in risk between least and most deprived only slightly and therefore PSA testing is probably not the only factor behind higher incidence of prostate cancer with increasing SES.<sup>116</sup> Lifestyle factors, which could also explain part of the effect, have not been sufficiently studied yet in this regard.

### Urinary tract cancers

Kidney cancer is roughly twice as common in men than in women.<sup>12</sup> Incidence is higher in more developed countries where it is on the rise.<sup>117</sup> Identified risk factors are for the most part life-style related, and are thus influenced by SES<sup>118,119</sup>, though within this review studies looking at the association between SES and kidney cancer have provided varied results (Supplementary tables 18 and 19). Nevertheless, it seems that more often than not, lower SES, measured most often as education or area deprivation, is associated with higher incidence in both sexes but slightly more strongly in women.<sup>19,33,36,59,120,121</sup> RRs are most often around 1.2–1.3 and rarely above 1.5. Controlling for risk factors was seldom performed. One study investigated the explanatory power of smoking and alcohol and found that smoking accounted for approximately 30% of the higher risk in low educated women, whereas higher alcohol consumption was apparently protective.<sup>33</sup> In Italy<sup>30</sup> and Lithuania<sup>32</sup>, the association was reversed, i.e. risk was increased with higher SES, while in France no association could be found.<sup>16,17</sup> The reason behind the reversed findings is not known, though may be due to advances in diagnostic activities.

Compared to women, bladder cancer rates are as much as five times higher among European men in whom it represents the fourth most commonly diagnosed cancer.<sup>12</sup> Like for kidney cancer, RRs comparing lowest and highest education are moderately elevated in lower educated men and women (Supplementary tables 20 and 21) and range up to 1.5 but are mostly between 1.2–1.3.<sup>16–19,27,30,32,120,121</sup> We could not identify any European study that

looked into how known and potential risk factors, primarily smoking and exposure to occupational carcinogens<sup>122</sup>, contribute to SES inequality in bladder cancer incidence. Considering smoking is such an important factor, most of the inequality is likely present on its account.

### Colorectal cancers

Colorectal cancer is strongly related to lifestyle and is the second most common malignant tumour (excluding non-melanoma) in Europe with respect to the absolute number of cases.<sup>12,123</sup> Incidence used to be higher among affluent Europeans<sup>2,124,125</sup> but a review of studies shown in Supplementary tables 20 and 21<sup>16–20,22,25–28,30–33,46,126–130</sup> has reinforced that in several countries, a reversal towards higher incidence among lower SES groups has occurred. For example, before the 1990s affluent Finnish men and women had an increased risk of colon and rectal cancers<sup>46</sup> but Finland has since seen a gradual narrowing of the educational gap, almost to the point of reversal, especially among men, which is due to relatively larger increases in incidence in lower SES individuals.<sup>127</sup> A similar pattern emerged in Norway.<sup>131</sup> In Denmark at the turn of the century, both colon and rectal cancers were already more common with greater individual disadvantage, particularly material and in men.<sup>126</sup> In Sweden<sup>128</sup> and Italy<sup>30</sup>, the lowest educated men and women now have up to about 30% and 15% increased risk for rectal cancer, respectively, with no differences for colon cancer. In the UK<sup>22,129</sup> and Germany<sup>18–20</sup>, area deprivation is associated with higher incidence of colorectal cancer as a whole, primarily in men. On the other hand, risk was lower in lower educated men and women in Lithuania for both colon and rectum<sup>31,32</sup>, while no clear association could be shown in Ireland<sup>28</sup>, the Netherlands<sup>26</sup>, France<sup>16,17</sup> and Iceland.<sup>25</sup>

### Melanoma and non-melanoma skin cancer

In Europe, skin cancer, including melanoma and non-melanoma (basal cell carcinoma – BCC and squamous cell carcinoma – SCC), has seen some of the fastest growing incidence rates among all cancers. For melanoma, body locations associated with the highest increases are limbs and trunk, which are intermittently exposed to sun radiation.<sup>132</sup>

Many studies in Europe (Supplementary tables 22 and 23) have found a positive association for melanoma and SES.<sup>16–19,21,25,27,29,30,32,33,36,59,133–138</sup> RRs

comparing the lowest to highest educated vary between 0.5–0.9 and are most often between 0.6–0.7. In a stratified analysis by body location, only melanoma of the limbs and trunk could be linked with SES.<sup>134</sup> When area-SES was investigated, RRs were slightly higher (around 0.8). This, along with the fact that in a study after mutual adjustment for individual-SES effect of area-SES could no longer be found<sup>29</sup>, points to individual SES as the primary factor for observed differences. Though controlling for risk factors has been scarcely attempted, high intermittent sun exposure among persons with higher SES could explain most of the gap. No study controlled for skin type in Europe, though populations in most countries are homogenous in this respect. Therefore, it is not surprising, for example, that in Norwegian women the number of sunburns accrued and latitude of residence explained most of the excess risk.<sup>33</sup>

Fewer studies were found for non-melanoma skin cancer (Supplementary tables 22 and 23). In Lithuania<sup>31</sup>, melanoma and non-melanoma showed equal RRs with respect to education and in Germany<sup>18</sup> non-melanoma cancer showed even stronger positive associations with area deprivation than melanoma though neither distinguished between SCC and BCC. In Denmark, BCC excess risk according to different indicators of high SES was virtually identical to RRs found for melanoma. SCC on the other hand was marginally associated only with higher income.<sup>133,139</sup> Conversely, in Nordic countries SCC was clearly more common in people with the highest education and occupational class<sup>36,140</sup>, while in Ireland<sup>141</sup> and Scotland<sup>137</sup>, along with BCC, SCC was also positively associated with area deprivation. This could mean that chronic exposure, which is generally considered higher in manual outdoor workers, is actually higher among the affluent, at least in the studied countries, or else they undertake more diligent screening.

### Lymphoid and haematopoietic cancers

Haematological cancers, the aetiology of which is unclear, are more frequent in males compared to females.<sup>142</sup> Overall, we could not confirm that these cancers are associated with SES (Supplementary tables 24 and 25).<sup>16,17,27,30,32,36,59,143,144</sup> In Italy<sup>30</sup>, risk of Hodgkin lymphoma was non-significantly reduced with RR around 0.8; elsewhere, no associations were found<sup>16,17,32,143</sup> or risk was higher in lower SES groups, such as among men with lowest education and male renters compared to owners in

Denmark<sup>144</sup> and in most deprived areas in England with RR of 1.6 for males and 1.4 for females.<sup>59</sup> Overall, non-Hodgkin lymphoma, multiple myeloma and leukaemia also do not seem to be associated with SES, excluding some reports of varied associations. In Germany, for example, risk for all lymphoid and haematopoietic cancers combined was higher in deprived men and women but this categorisation was too crude.<sup>19</sup> Authors of a report from the Haematological Malignancy Research Network in the UK concluded (aside from reporting on lower risk of myeloma in very deprived areas) that there are no SES inequalities for a myriad of disease entities categorised according to the detailed WHO classification.<sup>143</sup>

### Central nervous system cancers

Though rare, in adults gliomas and meningiomas are the most common tumours of the central nervous system (CNS).<sup>145</sup> The only well-established modifiable risk factor for CNS tumours is ionising radiation whereas at present there are no conclusive findings regarding exposure to non-ionising radiation (e.g. mobile phone use).<sup>146</sup> Within this review we could not confirm a clear association with SES (Supplementary tables 26 and 27). Given that CNS tumours encompass a variety of types, unsurprisingly, no clear direction of association could be ascertained when all types are analysed together. Thus, with increasing affluence, risk was increased in men in Denmark<sup>147</sup> and Sweden<sup>36</sup> and women in England<sup>59</sup>, decreased in men in Italy<sup>30</sup> and in parts of France<sup>17</sup> or else equal in France<sup>16</sup>, Germany<sup>19</sup>, Lithuania<sup>32</sup> and Norway.<sup>33</sup> Regarding specific types, there are some indications that glioma and acoustic neurinoma are less common with lower affluence while meningioma showed no unequal distribution according to SES.<sup>148-150</sup>

### Thyroid cancer

Influenced in part by improved detection of asymptomatic cancers, incidence of thyroid cancer is on the rise.<sup>151</sup> Our review (Supplementary tables 28 and 29) showed that thyroid cancer risk was greater among Lithuanian men and women with higher education (SIR between 0.8-0.9)<sup>32</sup> and in areas with lower deprivation in Germany (SRR between 0.6-0.7).<sup>19</sup> Risk was also increased, although not significantly, in highly educated Norwegian women (HR 0.7).<sup>33</sup> In other countries, researchers could not confirm this link<sup>16,17,59</sup>, whereas a study in Sweden found higher risks for lower educated



people.<sup>36</sup> Elevated risk in groups with higher SES could be explained by differential access to diagnostic procedures in favour of high-SES groups. Since there are no studies adjusting for multiple SES measures and risk factors, independent effects of different SES indicators as they relate to differing dimensions of SES (such as material, cognitive etc.) are as yet indeterminable.

## Conclusions

In our review we aimed to take stock of national or international studies that have investigated the link between the socioeconomic factors and cancer incidence, focusing specifically on Europe and studies based on cancer registry data published in the 21<sup>st</sup> century. It was necessary to consider two parts, one dealing with the social status (individual level) and the other with the social environment (neighbourhood level studies). It is evident that very few cancers are not associated with SES: head and neck, oesophagogastric, liver and gallbladder, pancreas, lung, kidney, bladder, penis and cervix are associated with low SES; conversely, high SES is associated with breast, prostate, thyroid and skin cancers. For other investigated locations, no associations were observed or else results are too few or varied to make firm conclusions.

Generally, negative associations are stronger for men than women and can be explained to a very large degree by known life-style related factors, most notably smoking as the single most important modifiable cause of a multitude of different cancers. Interestingly, the studies that mutually adjusted for either several different individual or individual as well as area SES measures have reinforced what has already been known, namely that: i) individual-level SES measures are not simply interchangeable but reflect different aspects of socioeconomic position, from material and cognitive to cultural; and ii) both area and individual SES have independent effects on cancer risk, again highlighting the complexity of the concept of socioeconomic status.

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