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# Testicular cancer: A narrative review of the role of socioeconomic position from risk to survivorship

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## Abstract

**Background—**Testicular cancer (TC) is one of the most curable cancers. Given survival rates of close to 100% with appropriate therapy, ensuring proper treatment is essential. We reviewed and summarized the literature on the association of socioeconomic position (SEP) along the cancer control spectrum from risk factors to survivorship.

**Methods—**We searched PubMed from 1966 to 2011 using the following terms: testicular cancer, testicular neoplasm, poverty, and socioeconomic factors, retrieving 119 papers. After excluding papers for the non-English (10) language and non-relevance (46), we reviewed 63 papers. We abstracted information on socioeconomic position (SEP), including occupation, education, income, and combinations of the 3. Five areas were examined: risk factors, diagnosis, treatment, survival, and survivorship.

**Results—**Most studies examined area-based measures, not individual measures of SEP. The majority of studies found an increased risk of developing TC with high SEP though recent papers have indicated increased risk in low-income populations. Regarding diagnosis, recent papers have indicated that lower levels of education and SEP are risk factors for later-stage TC diagnosis and hence higher TC mortality. For treatment, 1 study that examined the use of radiation therapy (RT) in stage I seminoma reported that living in a county with lower educational attainment led to lower use of RT. For survival (mortality), several studies found that men living in lower SEP geographic areas experience lower survival and higher mortality.

**Conclusion—**The strongest evidence for SEP impact on testicular germ cell tumor (TGCT) was found for the risk of developing cancer as well as survival. The association of SEP with TGCT risk appears to have changed over the last decade. Given the highly curable nature of TGCT, more research is needed to understand how SEP impacts diagnosis and treatment for TGCT and to design interventions to address disparities in TGCT outcomes and SEP. Published by Elsevier Inc.

### Keywords

Testicular cancer; Socioeconomic status; Socioeconomic position; Occupation; Income; Education

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## Introduction

Testicular germ cell tumors (TGCT), broadly classified as seminomas and nonseminomas, are the most common cancer in men between 20 and 39 years old and represent the leading cause of cancer-related morbidity and mortality in this age group [1]. TGCTs represent one-third of cancers among boys and young men between 15 and 29 years [2]. In 2007, more than 7,700 men were diagnosed and more 350 men died of TC in United States [3]. Incidence varies by country with the highest incidence rates in European countries [4]. With the introduction of platinum-based therapy in the 1970s, TGCT represents one of the most curable cancers with approximately 96% of men surviving 5 years or more today vs. 83% in the 1970s [5].

TGCT staging is based upon extent of disease at diagnosis, which includes lymph node status and whether distant metastases are present. After orchiectomy, careful work-up is done to determine clinical stage, histology of the tumor, and the need for treatment after surgery. Men with advanced disease are categorized into risk categories (good, intermediate, and poor) that represent site of metastases, histology, and the level of tumor markers ($\beta$ HCG and & $\alpha$ feto-protein) produced by the cancer [6]. Advanced seminomas are classified as good and intermediate risk (i.e., good/intermediate survival) and nonseminoma are classified as good, intermediate, and poor. Winter and Albers recently provided an excellent summary of treatment options in *Nature Reviews: Endocrinology* [7]. Treatment is based on stage at diagnosis as well as risk classification. Treatment interventions includes surgery, radiation therapy, chemotherapy, and close observation for men with stage I seminoma and nonseminoma. All men with advanced stage TGCT regardless of histology should receive chemotherapy. The extent of treatment is determined by risk classification [7]. For men with nonseminoma, those who do not respond to chemotherapy, salvage therapies such as stem cell transplant need to be considered.

## Relationship of socioeconomic position and cancer outcomes

For this review, we use the term “socioeconomic position” (SEP) as an encompassing term, inclusive of socioeconomic status, which indicates both resource-based and prestige-based indicators as defined by Krieger et al. and Galobardes et al. [8–10] According to Krieger et al., SEP indicators include “income, wealth, and educational credentials… as well as access to and consumption of goods, services, and knowledge, as linked to their occupational prestige, income, and education level” [10]. SEP, especially the lack of social prestige or resources, is associated with cancer outcomes for many types of cancer [11]. Many studies have examined race as a proxy for SEP in the United States [12–14]. As we were concerned about direct measures of SEP and previous papers have reported on racial differences in TGCT [2,15–17], this study does not include papers that focused only on racial disparities in TGCT risk, diagnosis, treatment, and survival. We concentrate our review on the association of SEP with risk factors for developing TGCT, as well as SEP differences in diagnosis, treatment, survival, and survivorship in TGCT patients.

## Literature review

We searched PubMed from 1966 to 2011 using the following terms: TC, testicular neoplasm, poverty, socioeconomic position, and socioeconomic factors, retrieving 119 papers. We initially excluded papers that were not written in English (10) and papers that were not relevant (46). We fully reviewed 63 papers and found that 41 papers [18–59] were relevant. Papers were further excluded for the following reasons: there was no SEP information reported in the paper (10), they were letters or commentaries (3), or they were older reviews (9). The reference lists of the remaining 41 papers were reviewed and 5 [60–64] additional papers were identified. We abstracted information on SEP, including occupation, education, income, and combinations of the 3. Five areas were examined: risk factors, diagnosis, treatment, survival, and survivorship.

## SEP and risk for developing testicular cancer

Cryptorchidism, familial and genetic factors, height, and early life/prenatal exposures have been suggested as risk factors for TC [65,66]. However, there is limited evidence of socioeconomic differences in these risk factors that may explain differences in incidence and survival from TC. While 1 study in the United States reported paternal SEP to be associated with a higher risk of cryptorchidism, a study in Nordic countries did not show SEP to be associated with cryptorchidism [67,68]. Familial and genetic factors play a role in the development of some TCs. However, only a limited number of specific susceptibility genes for TC have been identified [69,70]. Exposures early in life, including the prenatal period, have also been hypothesized to contribute to increasing TC risk [65,71]. However, literature examining the effect of these factors on population differences in TC incidence is limited.

Numerous studies report a higher risk of TC in men of high social class compared with men of lower social class [22,25,53,54,56,72,73]. However, more recent reports suggest that the association has decreased over time [55] and that the risk appears to be reversed with a higher risk of TC in men with lower SEP [52,55]. We also found that the change SEP differences have narrowed using testicular cancer incidence data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Program (Fig. 1). During 1973–2008, the age-adjusted TC incidence rate for persons living in high poverty areas was lower than the rate for those in low poverty areas, but increased at a faster rate. In 2008, the cancer incidence rate for persons living in high poverty areas (5.8/100,000) is approaching the rate for persons living in low poverty areas (6.2/100,000) in 2008.

Contrary to reports suggesting associations between TC incidence and SEP, others have found no evidence that SEP is associated with the risk for TC. Prener et al. found no association between socioeconomic class and risk of TC [51]. Similarly, the United Kingdom Cancer Study Group found no association between social class and TC risk [50]. Marsa et al. found no association between education, disposable income, and TC risk [49]. Parental SEP has a variable association with developing TC. Children of women with high SEP have been shown to have a higher risk of nonseminomas [54]. Paternal SEP has not been associated with an increased risk of TC [48,59].

While the literature does not consistently report an association between specific occupations and TC, numerous studies have examined this topic [21,47,74–76]. Occupation is defined in many ways, making comparisons difficult. Men with manual occupations and lower education have been found to have a higher incidence of TC [22,46]. Various studies have shown an increased risk of TC with numerous occupations, including metal workers, agricultural workers, and equipment technicians [21,42–45,77]. One study that examined chemical exposures reported an increased risk with fertilizers, phenols, and fumes [58]. Contrary to these studies, others have found no association between occupational exposure and TC risk [24,41]. Taken together, SEP in general, and occupation and education of parents, and at the individual level have shown variable associations with developing TC.

## SEP and stage at diagnosis

Few studies have examined SEP and stage at diagnosis among TC patients, and it is conceivable that patients with lower SEP and limited access to care would have delays in diagnosis [40,60]. Late stage diagnosis of TGCT, particularly nonseminomatous TC, has been shown to be a risk factor for increased TGCT-specific mortality [40,60]. We were able to find 2 studies that specifically address the association of stage at diagnosis of TC and SEP. Dieckmann et al. found that lower educational levels were related to delays in diagnosis for nonseminomatous TGCT in 180 German men [60]. In contrast, Toklu and colleagues reported on 140 Turkish men seen in their clinic from 1994–1995 and found that stage of diagnosis did not statistically differ by income level or between college graduates versus non-college graduates [40]. Recent SEER data (Table 1) showed that distant stage TC diagnoses are higher for persons living in areas of high-poverty >20% county poverty) and low educational attainment (>25% of men have not graduated from high school).

## SEP and treatment

Treatment for TGCT is multimodal with surgery, radiation therapy, and chemotherapy [7]. All of these treatments have varying side effect profiles, including infertility, chronic medical problems such as cardiovascular disease, neurotoxicity, nephrotoxicity, pulmonary toxicity from treatments, and second cancers and psychological problems [78]. Given the excellent survival among TGCT patients, treatment strategies continued to be explored that will reduce the toxicity of treatment while preserving long-term survival [79]. We did not find any studies of long-term side effects of TC treatment and SEP.

We found only 1 paper examining the association between treatment and county level SEP. This paper focused on adjuvant radiation therapy (ART) for stage I seminoma and county-level SEP [39]. Hoffman et al. reported that men living in counties with higher educational levels were more likely to receive ART after surgery. These findings are difficult to interpret as the treatment recommendations for stage I seminoma have evolved to the point where close follow-up after surgery is an acceptable alternative to ART [7]. We found no studies of TGCT treatment and individual-level SEP.

## SEP and survival

Although cisplatin was available starting in 1977, Fossa et al. note that it was not widely used until the mid-1980s [38]. Seven studies were reviewed on survival and SEP [18,37,38,49,62–64]. There were 2 distinct time survival periods based upon the availability of effective chemotherapy treatment with cisplatin. Davies analyzed a cohort of men diagnosed before the effective chemotherapy in 1975 and reported higher mortality in higher SEP populations [20]. Six studies examined SEP and survival in TC patients in the cisplatinera (after 1977) [18,37,49,62–64]. Sun et al. reviewed 22,553 TGCT cases in SEER databases from 1998–2006 and used a composite, area-based SEP score based upon median family income, percentage of individuals living below the poverty line, and percentage of individuals without a high school diploma. “Low” and “High” SEP categories were created using median score as the cut point. In multivariate analysis, individuals living in areas with “Low” SEP scores (vs. “High” SEP) had significantly higher cancer-specific mortality and overall mortality HR = 1.41 ($P = 0.002$) and 1.28 ($P < 0.001$), respectively [64]. Davies et al. also reported higher mortality for men with professional jobs [20]. Hussain et al. reported on 1,094 cases of TC in Swedish men diagnosed from 1990–2006. Men with 12–13 years of education had significantly lower HR of TGCT-specific mortality versus those with <9 years HR = 0.07 (95% CI 0.01–0.55). Yet this did not hold true for those with more than 13 years of education HR = 0.30 (95% CI 0.06–1.47) [62]. Nur and colleagues studied 18,605 men in England and Wales from 1986 to 1999 and found decreased survival in the most economically-deprived TGCT group compared with the most affluent group [37]. Power et al. reported similar results [18]. Conversely, Marsa et al. studied 1,770 Danish men from 1994–2003 and found no difference in 5-year survival rate with regard to disposable income, education, or employment status [49]. Similarly, Mackillop et al. did not find any significant TGCT survival differences by income level. [63]Overall, studies published to date have found that TGCT mortality and survival has markedly improved with cisplatin-based chemotherapy but a gap remains between survival in high versus low-SEP populations. Current SEER data confirm these findings (Table 1). Men with TC diagnosed in counties with high poverty and low educational attainment have lower survival compared with their counterparts. These effects were especially strong for men over 40 years similar to reports from Fossa et al. [38].

## SEP and survivorship

Studies have shown that TC survivors experience a variety of negative psychosocial outcomes following diagnosis and treatment of TGCT [57,80–82]. The issue of quality of life is particularly important among TC survivors as they are often diagnosed at a younger age. Over 80% of boys and men with TGCT are between 14 and 44 [2]. This makes infertility an issue for TC survivors [78,83], but we found no studies that described the association of infertility and SEP. Distress about loss of fertility as a psychosocial outcome is addressed by 1 of the articles in our review. For this review, we identified 8 articles that examined how psychosocial outcomes are influenced by SEP in TC survivors [29–36]. The relationship between psychological outcomes and SEP was not consistent in TC survivors. While Skaali et al. [33] and Tuinman et al. [29] did not find that SEP was associated with TC-related distress and mental health, respectively, in survivors, others have reported an

association between lower SEP and poor psychological outcomes. Fleer et al. investigated cancer-related stress symptoms in The Netherlands [36]. The study showed that survivors with less education and without paid employment were more likely to experience cancer-related distress and higher levels of avoidance coping. Rutskij et al. also found that lower levels of SEP measured as less than 12 years of schooling was associated with an avoidance coping style in a univariate model. Multivariate analysis using these data showed a small, significant association between not being in paid work and approach coping; there was no significant association between education and coping strategy [34]. Using data from the same study of Norwegian survivors, Skaali et al. found that unemployment, men with 12 or fewer years of education, and economic problems were significantly associated with fear of recurrence [32].

Rieker et al. reported that men with less than a college education, lower income, and lower occupational status experienced higher rates of distress about loss of fertility. Lower educational level and occupational status were also associated with higher sexual performance distress [35]. In a study of cancer survivors of many cancer types, Taskila et al. reported that male cancer survivors with less than a college degree and lower occupational status had a greater need for support in the workplace and from occupational health personnel [31]. The same authors found that male cancer survivors with a university degree were 10 times less likely to report impairment of ability to work than male cancer survivors who had the lowest level of education [30].

## Conclusion

Testicular cancer represents a modern medical triumph with more than 95% of men living 10 years or more [78]. This has been made possible through advances in diagnosis and treatment. We found evidence that socioeconomic position is associated with TC risk, diagnosis, treatment, survival, and psychological outcomes among men who are cured. Given the younger ages of adolescents and men affected by TC, long-term physical and psychological outcomes must be addressed as well. As with other cancers, there is evidence that TC outcomes are worse in older persons [78] and minorities, especially African Americans [64]. Access to care and receipt of state of the art treatment should be given to ensure equitable outcomes.

We have identified SEP gaps along the cancer spectrum from risk of developing TC to psychological outcomes. Why has there been a shift in the occurrence of TC in lower SEP populations? Over time, researchers have noted that the incidence gap between higher and lower SEP groups has narrowed, which is illustrated by SEER data in this paper. How do these changes relate to the etiology of TC? At the point of diagnosis, men of lower SEP are diagnosed at a later stage of cancer and have a lower survival. What role does increased awareness among providers and patients play in closing these gaps? Very little data exist about treatment differences by SEP and outcomes. More research is needed elucidate the determinants associated with treatment and whether these differ by SEP. We noted an almost 10% difference in 5 year survival for men over 40 years diagnosed with TC living in counties with >20% poverty rates compared with those living in counties with <10% poverty.

Men of lower SEP may have fewer resources at their disposal to deal with the diagnosis, treatment, and long-term physical effects of their treatment. Though cured, men will need to be enrolled in a surveillance program to prevent new problems and diagnose complications early. For example, men surviving TC have an observed to expected ratio of heart attack of 7.1 (95%CI: 1.9–18.3) compared with controls [78]. Surveillance programs are being put into place and more research is needed to provide the evidence-base to provide the best care [78].

Opportunities for research in TC spans the spectrum from elucidating risk to designing evidence-based survivor follow-up models. Future research should both verify the findings presented in previous studies and provide an evidence basis for interventions thought to be helpful in addressing the disparities noted in this review.

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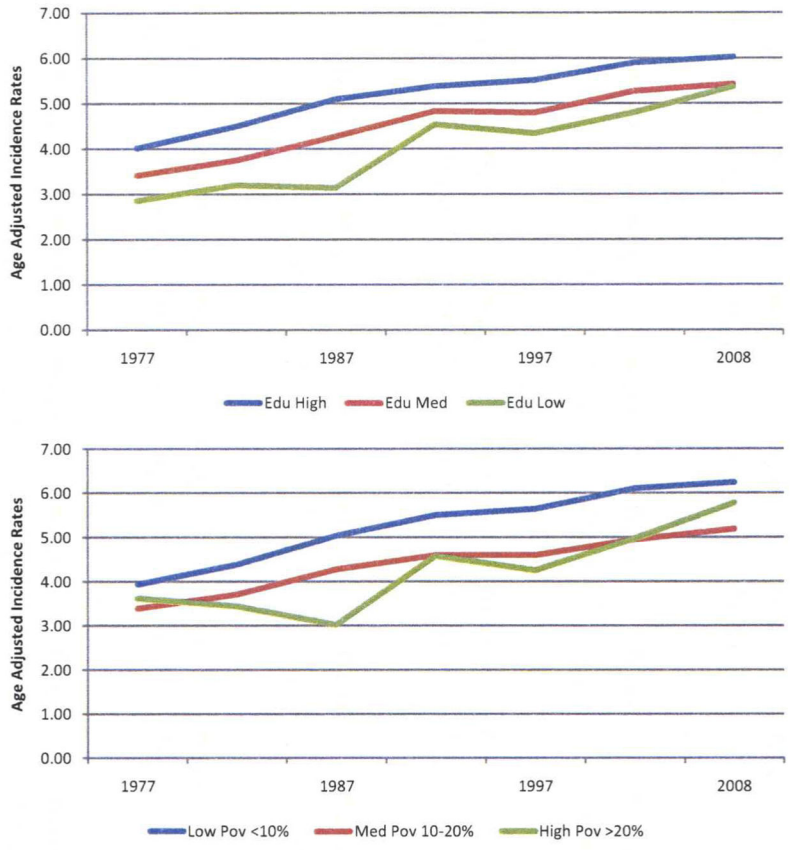


**Fig. 1.**

Trends in testicular cancer incidence by county socioeconomic measures*, Surveillance, Epidemiology, and End Results (SEER) (9 registries), data, 1975–2008. Rates were calculated as 5-year moving averages and were age-adjusted to the 2000 U.S. standard population. Data were released in April 2011 and based on the November 2010 submission (http://www.seer.cancer.gov/resources/). *Educational attainment: Low is defined as ≥25% of men without a high school diploma. Medium is defined as 15%–24.9% of men without a high school diploma. High is defined as <15% of men without a high school education. Poverty: High is defined as ≥20% of individuals below the poverty level. Medium is defined as 10%–20% of individuals below the poverty level. Low is defined as <10% of individuals below the poverty level. (Color version of figure is available online).

**Table 1**

Testicular germ cell tumor stage at diagnosis (2000–2008) and 5-year relative survival rates (2000–2003) by socioeconomic position, surveillance, epidemiology, and end results (SEER) (17 registries) data

| | County-level poverty* | | | | County-level education attainment** | | | |
|---|---|---|---|---|---|---|---|---|
| | **High** | **Medium** | **Low** | ***P* value** | **Low** | **Medium** | **High** | ***P* value** |
| SEER summary stage at diagnosis | | | | <0.01 | | | | <0.01 |
| Localized | 68.0% | 69.8% | 73.0% | | 68.0% | 71.2% | 73.4% | |
| Regional | 17.3% | 17.9% | 17.5% | | 18.2% | 17.6% | 17.5% | |
| Distant | 14.7% | 12.2% | 9.5% | | 13.8% | 11.2% | 9.1% | |
| 5-year relative survival by Age | | | | <0.01 | | | | <0.01 |
| Age < 40 | 93.5% | 95.0% | 96.9% | | 93.9% | 95.5% | 97.6% | |
| Age ≥ 40 | 87.6% | 94.1% | 96.9% | | 91.9% | 94.9% | 97.6% | |

Data were released in April 2011 and based on the November 2010 submission (http://www.seer.cancer.gov/resources/).

* Poverty: High is defined as ≥20% individuals below the poverty level. Medium is defined as 10%–20% individuals below the poverty level. Low is defined as <10% individuals below the poverty level.

** Education attainment: Low is defined as ≥25% of men without a high school diploma. Medium is defined as 15%–24.9% of men without a high school diploma. High is defined as <15% of men without a high school diploma.