

# Impact of Socioeconomic Status on Prostate Cancer Outcomes Globally: A Protocol for Systematic Review and Meta-analysis

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**Keywords:** Prostate neoplasm, Prostate cancer, Recurrence, Mortality, Prevalence, Quality of life, Secondary treatment, Socioeconomic status, Income, Outcome

**Posted Date:** November 19th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-109558/v1>

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# Abstract

## Background

One in every four men will be affected by prostate cancer. Choice of treatment depends on factors including grade and stage of the disease, age of the patient, availability of treatment options and socioeconomic status. We aimed to develop a protocol to assess the impact of socioeconomic status on prostate cancer outcomes globally.

## Methods

A search strategy is developed using MeSH, text words, and entry terms. Nine databases will be searched, including PubMed, African Journals Online (AJOL), Google Scholar, Scopus, Cochrane Library, CINAHL, Web of Science, Embase and ResearchGate. Only observational studies, retrievable in the English language will be included. The primary outcome of this study is the socioeconomic status of prostate cancer patients. Secondary outcomes include mortality due to prostate cancer, health related quality of life, prostate cancer recurrence, need for secondary treatment, time to return to work, treatment choice regret and hospice enrollment. Identified studies will be screened and selected based on inclusion criteria. Data items will be managed in Zotero software, Microsoft Excel and CMA software. Both quality scores and the risk of bias for individual studies will be reported. Studies will be assessed for methodological, clinical, and statistical heterogeneity. Funnel Plots will be used for assessing publication bias.

## Discussion

This protocol will enable a transparent, reliable and accurate method for assessing the impact of socioeconomic status on the global prostate cancer outcomes. It will allow discussions on outcomes such as mortality due to prostate cancer and how income disparity and availability of treatment options can influence prostate cancer outcomes. The final report of this study will be published in a peer-reviewed journal and the findings will be made available to health authorities.

## Systematic review Registration

This protocol has been registered in PROSPERO, with registration number CRD42020213700

## Background

Globally, the incidence of prostate cancer has been on the increase over the years. Marked by differences in epidemiology, the prevalence varies with geographical location and its incidence progressively increases with age [1]. The incidence was reported to be higher in countries with higher socioeconomic development [1]. It constitutes a significant burden of non-skin cancers in men as the second most commonly diagnosed cancer in adult males and ranked the sixth leading cause of cancer-associated male mortality globally in 2018 [2]. It is a common condition and the lifetime risk of being diagnosed with prostate cancer was observed in a study to be approximately 1 in 8 for White men, 1 in 4 for Black men,

and 1 in 13 for Asian men, whereas that of dying from prostate cancer is approximately 1 in 24 for White men, 1 in 12 for Black men, and 1 in 44 for Asian men [3]. It is also thought to be more aggressive in black men compared to men of other races [4]. This disease has attendant morbidity, mortality, poor quality of life, psychological challenges [5], high cost of treatment, poor treatment free survival rate [6] which are some of the sources of concern in these patients. These concerns are at times compounded depending on the socioeconomic status of the patient.

The treatments can be financially demanding, involving but not limited to radical prostatectomy, radiotherapy, both medical and surgical castration [7] among others and depend on the disease risk category derived from combination of patient's prostate specific antigen level (PSA), Gleason score and Tumour stage with various modifications [8, 9]. Therefore, it poses a threat to overall health related quality of life of the subject and his dependents including the spouse [10]. In the early stage disease, treatment is aimed at cure thus preventing morbidity and mortality while for late stage, it is palliation with improvement in overall quality of life.

Socioeconomic status especially where there is no health insurance coverage may constitute a barrier to decision to seek early intervention, proper patient evaluation, choice of treatment and post treatment follow up which can negatively affect the disease outcome in terms of prognosis and patient overall treatment free survival.

Numerous factors are associated with prostate cancer outcome evaluation. These include proportion of prostate cancer specific deaths, degree of Health related quality of life (HRQOL) [10–13], proportion who regret choice of treatment for prostate cancer [14–16], incidence of and mortality rate of those with 'unknown risk' category for prostate cancer, incidence rate of prostate cancer, disease-free time, positive surgical margin, proportion of those needing hospice enrollment [17], proportion of those who needed secondary treatment [18], socioeconomic class, medical Insurance status [11, 12, 18], income and education [19]. Lack of health insurance coverage [18] and low socioeconomic class are related to poor HRQOL and worse prostate cancer outcome [18, 20, 21].

The negative impact of a patient's socioeconomic status with regard to prostate cancer outcome has been reported in some studies [11]. But even where access to health care coverage was provided, it has been reported that socioeconomic status did not correlate with prostate cancers outcome [22]. Furthermore, it was observed that with access to health care coverage and irrespective of treatment option offered to men with low risk localized prostate cancer, a higher number of men still died from lower compared to higher socioeconomic groups, though the finding was not significant [23]. Another study also noted in their analysis that sociodemographic factors were not important prognostic factors in determining outcome after External Beam Radiation Therapy (EBRT) for prostate cancer [24]. While another study found increased relative risk for presenting with advanced-stage prostate cancer in Hispanic but not in African-American men to be related to traditional socioeconomic, clinical, and pathologic factors [25, 26]. Therefore, there is a need to determine the significance of variation in patient socioeconomic status and prostate cancer outcomes. This will fill the gap in knowledge on the

relationship between patients' socioeconomic status and prostate cancer outcome. This protocol is therefore developed to conduct a systematic review and meta-analysis on the impact of socio-economic status of prostate cancer patients on their disease outcomes using published primary studies.

## Methods And Design

The main objective of this protocol is to determine the impact of socioeconomic status on the outcomes of prostate cancer globally.

### Study objectives

1. To compare the mortality due to prostate cancer among different socioeconomic classes.
2. To determine the impact of socioeconomic status on the choice of treatment, rate of recurrence, time to return to work, HRQOL and rate of secondary treatment

### Review questions

1. Does socioeconomic status affect prostate cancer outcomes?
2. Does socioeconomic status affect the choice of prostate cancer treatment?
3. Are prostate cancer outcomes moderated by mean income, educational status, race, and medical insurance status?

### Study Design

This is a protocol for systematic review and meta-analysis of observational studies that reported the impact of socioeconomic status on the outcome of prostate cancer worldwide. Other types of study designs are excluded including interventional studies, comments and editorials. There is no time restriction on eligible primary studies.

### Inclusion criteria are:

- a. Observational studies (cohort, cross-sectional, case-control, historical cohort)
- b. Studies of all years that are published and or retrievable in the English language
- c. Studies that are available in electronic databases.
- d. Studies that report socioeconomic status impact on any of the prostate cancer outcomes (the primary outcome is socioeconomic status of prostate cancer patients) and/ or secondary outcomes such as mortality, survival, HRQOL, recurrence, choice of treatment regrets and time of return to work.

### Exclusion criteria are:

- a. Narrative reviews, interventional and experimental studies
- b. Letters to the editor

- c. Studies that are not reported or retrievable in the English language
- d. Studies without data on socioeconomic status of prostate cancer patients.
- e. Grey literature will not be included.

## **Study characteristics**

The PICOS is as follows

**Participants:** men with prostate cancer worldwide

**Intervention:** There is no intervention

**Comparator:** There is no comparator

**Outcome:** The primary outcome is socioeconomic status (SES) of prostate cancer patients. The measurable secondary outcomes are mortality, HRQOL including depression and time of return-to-work, recurrence, need for secondary treatment, treatment choice regret, unknown risk category and hospice enrollment. Filters used for subgroups are SES, income, education, insurance and race.

## **Information sources**

The search will employ sensitive topic-based strategies designed for each database. The nine databases to be searched are CINAHL, PubMed, Web of Science, Google Scholar, African Journal Online, Scopus, ResearchGate, Embase, and Cochrane Library. The study will include only observational studies retrievable in the English language.

There is no time frame/restriction in the inclusion of publications.

## **Search strategy**

The search strategy included MeSH terms, text words and entry words. The search strategies that were used are shown in Table 1.

## **Data Extraction and Management**

Three tools will be used for data extraction and management: i) Zotero software, ii) Microsoft Excel and iii) Comprehensive Meta-analysis software CMA version 3

**a) Screening:** Studies will be screened at four levels:

Level 1: screening to select only observational studies while other study designs are excluded.

Level 2: screening titles and abstracts of observational studies using MeSH terms, keywords, and entry terms.

Level 3: screening of the selected studies by full-text reading, using the same strategy

Level 4: snowballing of the literature using included studies

**b) Reviewers:** Fifteen reviewers are involved in this study. Two reviewers will independently screen studies from each database and assess studies for inclusion and or exclusion. Conflicts will be resolved by a third reviewer. All reviews are blinded.

**C) Selection process:** The screening and deduplication will be done in Zotero software. Studies will be selected based on eligibility criteria and primary measurable outcome. Authors of studies with missing data will be contacted via email and telephone.

**d) Data collection:**

The following data items will be extracted from each eligible study into Microsoft Excel:

- i. first author's surname and year of publication of the study,
- ii. socioeconomic status: income, educational level, insurance status
- iii. prostate outcomes: mortality due to prostate cancer, HRQOL including depression and time of return-to-work, recurrence of the prostate cancer, need for secondary treatment, treatment choice regret, unknown risk category, and hospice enrollment,
- iv. sample size.

Data from Microsoft Excel will be exported to CMA software for meta-analysis

**Data items (Main measurable outcomes)**

The measurable data items in this study are:

- i. socioeconomic status including numerical data such as income, categorical data such as educational status, and categorical data such as health insurance status. The effect size is mean or median income status.
- ii. prostate cancer-specific mortality rate (categorical data), prostatic cancer recurrence rates (numerical data), health related quality of life (numerical data), recurrence of prostate cancer (categorical), choice of treatment regrets (categorical), and time of return to work (numerical)

**Risk of bias**

The risk of bias in included studies will be accessed for the individual studies using the National Institute of Health (NIH) Quality assessment tool for observational cohort and cross-sectional studies. This will be cross-checked with the Cochrane tool of risk of bias assessment for the strength of the body of evidence, i.e., using specific relevant items from this tool to assess the strength of the body of evidence.

Studies with extreme bias may be excluded after assessment in the following areas:

1. Method of testing and reporting at the outcome level
2. Heterogeneity will be assessed at the study level
3. Publication bias will be assessed at the study level
4. Sensitivity test using include/exclude function in the CMA software will be done at the study level

## Data synthesis

- A. Studies that passed the methodological quality assessment using the NIH quality assessment tool will be extracted. The results will be presented in tabular format in addition to a narrative synthesis.
- B. The following shall be included in the meta-analysis:
  - i) Report on socioeconomic status. Mean income status will be expressed in cohen's d as the effect size.
  - ii) Subgroups analysis will be done using moderators such as educational status, insurance status, treatment option, race, recurrence of prostate cancer and choice of treatment regret.

Eligible studies will be quantitatively analyzed using the Comprehensive Meta-analysis CMA Software, Version 3 (BioStat USA). The random effect model will be used for computation.

In addition to subgroup analysis, a meta regression will be performed using numerical independent variables such as time to return to work, patients age and health related quality of life while income status will be the outcome variable.

A cumulative meta-analysis will be performed to check for trends on SES and prostate outcomes over years.

## Assessment of Meta-bias

To test for heterogeneity Q value,  $I^2$ ,  $T^2$  will be used.  $I^2$  values of less than 40% will be considered low heterogeneity, values > 40 to  $\leq 75$  % moderate while values > 75% are high. Publication bias will be assessed using a funnel plot and test of asymmetry. Sensitivity test using include /exclude function will be performed in the CMA software.

## Results

The study selection process will be summarized in a flow diagram according to the PRISMA 2015 Statement and PRISMA-P Checklist (attached). A table of the search strategy in various databases showing text words, MeSH, and entry terms will be included. A list of included studies will be summarized in a table. Pooled cohen's d for socioeconomic status, standard error, and 95% CI, P values, and relative weights assigned to studies and heterogeneity tests will be included in forest plots. A table of quality scores and risk of bias of each eligible study will be included. Forest plots to show sub-group analysis will be included. A cumulative meta-analysis to check for trends will also be included.

## Discussion

The impact of socioeconomic status on prostate cancer outcomes will be discussed. The regression model from meta-regression will be examined for the predictive factors. The various changes in effect size due to sensitivity test will also be discussed. The final study will be published in a peer-review journal and the findings will be submitted to the Ministry of Health to inform policy decision making.

## Abbreviations

AJOL African journal online

CINAHL Cumulated Index to Nursing and Allied Health Literature

CMA Comprehensive Meta-analysis

EBRT External beam radiation therapy

HRQOL Health related quality of life

NIH National institute of health

PSA Prostatic specific antigen

PRISMA Preferred Reporting Items for Systematic Reviews and Meta- Analyses

## Declarations

- **Ethics approval and consent to participate:** The protocol does not require ethical approval due to the nature of the study design. It uses already published studies.
- **Consent for publication:** All reviewers/investigators consented to publication
- **Availability of data and materials:** Data and supplementary materials will be available to the public unhindered.
- **Competing interests:** The authors declare no competing interests
- **Funding:** Funding for the study will be provided by the Association for Good Clinical Practice in Nigeria AGCPN
- **Role of Funder:** AGCPN provided the platform for design and development of the protocol.
- **Guarantor of the Review:** Dr Emmanuel Nna
- **Contributors:** EN conceived the project, EN, EBU, ODC, AU, AK, OCE, ICR and MG designed the study. EBU and GMA did PubMed searches, screening and review; ODC and IR did AJOL searches and review; AU, AK and OCE did Google scholar searches and review; AAI, UIB and MIA did searches and review for CINAHL, ODC and EBU did Scopus and Web of Science searches, screening and review,

KKN and AU did Cochrane Database searches, screening and review while AR and EBU did review of ResearchGate

- **Acknowledgements:** We thank Dr Sam Ibeneme for his advice.

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# Table

Table 1:

Search strategy

S/N	DATABASE	SEARCH STRATEGY
1	PUBMED	((Prostate Neoplasm* OR Prostatic Neoplasm OR Prostate Cancer* OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate) OR "Prostatic Neoplasms"[Mesh]) AND ((Social Classes OR Socioeconomic Status OR Socioeconomic Factors) AND "Outcome")
2	GOOGLE SCHOLAR	(Prostate Neoplasm* OR Prostatic Neoplasm OR Prostate Cancer* OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate) OR "Prostatic Neoplasms) AND ((Social Classes OR Socioeconomic Status OR Socioeconomic Factors) AND "Outcome")
3	AJOL	(Prostate Neoplasm* OR Prostatic Neoplasm OR Prostate Cancer* OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate) OR "Prostatic Neoplasms) AND ((Social Classes OR Socioeconomic Status OR Socioeconomic Factors) AND "Outcome")
4	COCHRANE	Prostate Neoplasm? OR Prostatic Neoplasm OR Prostate Cancer? OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate OR Prostatic Neoplasms AND Social Classes OR Socioeconomic Status OR Socioeconomic Factors AND "Outcome"
5	WEB OF SCIENCE	Prostate Neoplasm? OR Prostatic Neoplasm OR Prostate Cancer? OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate OR Prostatic Neoplasms AND Social Classes OR Socioeconomic Status OR Socioeconomic Factors AND "Outcome"
6	CINAHL	Prostate Neoplasm? OR Prostate Cancer? OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate AND Social Classes OR Socioeconomic Status OR Socioeconomic Factors AND "Outcome"
7	SCOPUS	"Prostate Cancer? OR AND Socioeconomic Status AND "Outcome""
8	RESEARCH GATE	Prostate Neoplasm? OR Prostate Cancer? OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate AND Social Classes OR Socioeconomic Status OR Socioeconomic Factors AND "Outcome"
9	EMBASE	Prostate Neoplasm? OR Prostate Cancer? OR Cancer of the Prostate OR Prostatic Cancer* OR Cancer of Prostate AND Social Classes OR Socioeconomic Status OR Socioeconomic Factors AND "Outcome"

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