ENSIGN GLOBAL COLLEGE

KPONG, EASTERN REGION, GHANA

FACULTY OF PUBLIC HEALTH

DEPARTMENT OF COMMUNITY HEALTH

PROSTATE CANCER DETERMINANTS, DISEASE SEVERITY AND TREATMENT OUTCOMES AT THE SWEDEN GHANA MEDICAL CENTER IN THE GREATER ACCRA REGION OF GHANA

By

FRANK OBENG

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SEPTEMBER, 2023

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A THESIS SUBMITTED TO THE DEPARTMENT OF COMMUNITY HEALTH, FACULTY OF PUBLIC HEALTH, ENSIGN COLLEGE OF PUBLIC HEALTH IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE

MASTER OF PUBLIC HEALTH DEGREE

SEPTEMBER, 2023

DECLARATION

I hereby declare that except for reference to other people's work, which I have fully cited, this project submitted to the Department of Community Health, Ensign Global College, Kpong; are the results of my own investigation and has not been presented elsewhere for any other degree.

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--FRANK OBENG

LIST OF ABBREVIATIONS AND MEANINGS

ALC – Alcohol

ATG – Additional/Adjuvant Treatment Given

BMI- body mass index (Weight/Height^2)

BMI: Body Mass Index

CT: Computed Tomography

CXR: Chest X-ray

DRAD – Dose of Radition

DRE: Digital Rectal Examination

DRE_CD – DRE Coded

ETH – Ethnicity

FMH – Family History

FPSA – Fail PSA

FRM – FAIL Refractory Multiples

HPSA – Highest PSA During Treatment

HSD3B2 -- 3-beta-hydroxysteroid dehydrogenase type 2 enzyme

HT – Hormone Therapy

ISUP: International Society of Urological Pathology

LIN W-H – Linear (Weight/Height)

LIN_CAT - Linear Weight- To- Height Category

LOC – Location

LOC_CD – Location Coded

LPSA – Lowest PSA

MRI: Magnetic Resonance Imaging

MRT – Marital Status

NATG – Number Of Additional/Adjuvant Treatment Given

OCC_ACT – Occupation Based-Activity Level.

OCC_SES – Occupation-Based Socio- Economic Status

OCC_TRD – Occupations as Traditionally Classified

PET: Positron Emission Tomography

PLR – Place of Residence

PND – Ponderal Index Weight/Height^3)

PSA – PSA at Diagnosis

PSA: Prostate-Specific Antigen

PSAD - PSA Resolution Per Dose Of Radiation

PSAD_CD - PSA Resolution Per Dose of Radiation Coded

PSATM - PSA Resolution Per Number Of Treatment Modality

ROC: Receiver-Operator Characteristic

RPSA – PSA Resolution Under Treatment

TBC – Tobacco

TMG – Total Number Of Modalities of treatment Given

TRISK – T Stage Risk

TRUS: Transrectal Ultrasound

USG: Ultrasonography

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ABSTRACT

Background: Prostate cancer is a global health concern, with varying epidemiological patterns across populations. This study investigates the demographic/physical attributes, disease characteristics, and treatment outcomes of prostate cancer patients at the Sweden Ghana Medical Centre (SGMC) to provide insights into the Ghanaian context.

Methods: An analysis of retrospective data from 852 prostate cancer patients who visited SGMC from 2011 to 2023 was conducted. Demographic information, which included age , ethnicity, marital status, occupation, socio-economic status, level of activity, place of residence, family history, alcohol consumption, and tobacco use, was assessed. Disease characteristics included clinical stage, risk stratification, and PSA levels . Treatment outcomes studied included, PSA response and incidence of toxicity. Descriptive statistics, correlation analysis, logistic regression analysis plus modelling was done and odds ratios calculated; all at an alpha of 0.05%.

Results: Mean age was 67.5 years; median was 68.0 years. Median PSA at diagnosis was 29.0 ng/ml. There were notable variations in weight (mean 76.8 kg, SD 12.7), height (mean 1.71 meters, SD 0.07), and body mass index (BMI) (mean 26.3 kg/m², SD 4.1). Ethnicity, was predominantly Akan (55.52%), Ga (13.38%), Ewe (14.91%), men from Northern Ghana (6.34%), Nigerians (8.57%), Other Africans/Jamaicans (0.95%), Caucasians/Asians (0.34%). Patients, aged > 65 years, (OR = 2.34, p = 0.022) and high BMI (OR = 2.34, p = 0.022), were associated with high PSA; and BMI alone, with high risk localised prostate cancer, but a reduced propensity to metastatic prostate cancer. Ga and Ewe Ethnicities were associated with low risk localised prostate cancer on DRE (OR = 0.52, p = 0.049). High socio-economic status (59.32%) and sedentary occupations (56.5%) predominated. Urban residence was prevalent among patients (74.79%), with a noteworthy number of foreigners (10.18%). Family history (24.65%), alcohol consumption (31.3%), and tobacco use (8.6%) exhibited varying prevalence rates. Comorbidities were relatively uncommon, but with hypertension being the most frequent (10.55%).
Late diagnosed prostate cancer was commonplace; 46.81%. Metastatic prostate cancer rate was 28.72% of cases. Risk stratification indicated a considerable proportion of overall high-risk disease in patients with localised disease (44.75%). External beam radiotherapy was the primary treatment modality (76.88%), often combined with hormonal therapy (55.06%). The mean PSA response per unit of treatment dose was 31.60 ng/ml per Gray; and response rate was 53.16%. Treatment toxicity was infrequent (6.09%). Overall survival and quality of life data were however, not available. PSA, BMI, DRE, ISUP, predicted metastasis-probability in prostate cancer in a mathematical model with Sensitivity of 85.65%; Specificity of 95.45%; Positive Predictive Value of 90.84%; Negative Predictive Value of 92.65% and an accuracy of 75.31%. AUC of ROC curve = **90.55%;** $YIELD_p$= **68.71% and** $YIELD_s$= **95.45%.** A prostate cancer case-detection model which estimates an individual's prostate cancer risk(between 0 and 1) using PSA, BMI, linear weignt-to height ratio, age, marital status, ethnicity, family history of prostate cancer, socio-economic status, tobacco use and sedentary, or non-sedentary occupation in one model, was also obtained. It outperformed a PSA alone model, considerably.

Conclusions: Though limited by secondary data, Age, BMI, Ethnicity, marital status, occupation, and socio-economic status were identified as key determinants. Aggressive preventive measures on all fronts are are needed to diagnose more early stage prostate cancer, nationally, to improve prostate cancer outcomes.

Keywords: Prostate cancer, trends, determinants, risk-estimator, treatment outcomes.

CHAPTER 1

1.0 INTRODUCTION

1.1 Background of Study

Prostate cancer's higher occurrence among African-African and African American men is a widely recognized fact within the field of public health and clinical professionals dealing with prostate cancer patients (Hsing et al., 2014). Factors influencing prostate cancer include age, family history, genetics, diet rich in fats, obesity, elevated body mass index (BMI), and lifestyle factors like smoking and alcohol consumption (Rawla et al., 2019; Castro et al., 2015; Bagnardi et al., 2015; Rider et al., 2016). However, investigations into potential hereditary links in Ghana remain limited, leaving unexplored the possible variations in prostate cancer incidence across different ethnic and demographic groups in the country (Yeboah et al., 2009). The aim of this study is to bridge this gap by examining if there's any distinct clustering of prostate cancer cases in terms of case frequencies or rates, disease risk profiles, stage at presentation/diagnosis, and treatment outcomes among various ethnic and demographic groupings in Ghana, represented conveniently by the population of prostate cancer patients accessing the Sweden Ghana Medical Center, Accra.

Considering prostate cancer as the primary cause of male cancer-related deaths in Ghana (Wiredu and Armah, 2006; Laryea et al., 2014) and with only 15 percent of cases being diagnosed at an early curable stage (Globacon statistics, 2020), the urgency for robust health promotion efforts becomes clear. Effective health promotion relies on locally derived statistics; this emphasizes the significance of studies like this one that seeks to establish links between Ghana's ethno-demographic groups and the clustering of prostate cancer.

Ghana is characterized by its multi-ethnic composition, with over seventy distinct ethnic groups. Key ethnic groups include the Akan (47.5% of the population), Mole-Dagbon (16.6%), Ewe (13.9%), Ga-Dangme (7.4%), Gurma (5.7%), Guan (3.7%), Grusi (2.5%), Kusaasi (1.2%), and Bikpakpaam (a.k.a. Konkomba

people, 3.5%) (2021 Ghana Population and Housing Census). In the context of ethnic disparities in prostate cancer, Rebbeck et al. (2022) found varying frequencies for certain genetic variants among ethnic groups, such as V89L (which indicates a mutation or change from the amino acid Valine to the amino acid Leucine at position 89 of the androgen receptor protein) and CYP3A4*1B (Cytochrome P450 3A4, variant 1B).

Earlier research, extending back to Sunita et al. (1998), suggests that elevated dihydrotestosterone (DHT) levels might heighten prostate cancer risk. The HSD3B2 (3-beta-hydroxysteroid dehydrogenase type 2 enzyme) gene's role in DHT (dihydrotestosterone) inactivation has been implicated in prostate cancer pathogenesis. Even older Asian and Nigerian studies by Pu et al. (2010) and Ekwere and Egbe (2002), respectively, demonstrate shifting prostate cancer incidence trends among different ethnicities. Despite these references, a comprehensive Ghanaian study remains outstanding. PSA as a marker of prostate cancer is very useful, yet still limited in predicting prostate cancer(it is not perfect; and its dynamics in Africans is even, more complex). This makes enquiry into other markers and additional determinants that could better PSA's utility very essential (Catalona et al, 2014). The phi index (Catalona et al, 2014) has tried to improve this situation; but has ended up deepening health disparities by creating an index that relies on expensive tests (PSA, free PSA, pro PSA), making the ordinary Ghanaian/African not an everyday beneficiary of it. There is therefore the need for local research to explore ways of making PSA more useful to the local health systems, by combining it with some physico-demographic features in models that may help predict/detect prostate cancer disease, gauge disease severity and treatment outcomes in more efficient ways (Wiredu and Armah, 2006).

In conclusion, this study's purpose is to make an attempt at addressing the gap in understanding the potential variations in prostate cancer clustering among Ghana's diverse ethnic and demographic groups, and the possible effects of the differences, on disease severity and treatment outcomes amongst the patients that access the Sweden Ghana Medical Center for prostate cancer care. This endeavor holds importance due to Ghana's prostate cancer burden and the need for tailored health promotion efforts based on sound local research.

1.2 Problem Statement

Prostate cancer presents a significant public health challenge; afflicting the male population in Ghana, with substantial implications for male mortality. The incidence of prostate cancer in Ghana is alarmingly high, with 2,129 reported cases in 2020, resulting in 1,117 fatalities (52.5% Case Fatality Rate), making it the leading cause of cancer-related deaths among men in the country (Globacon, 2020). This issue is particularly concerning for Ghana's population aged 40 and above.

Several critical factors contribute to the severity of the problem:

1. **Late Presentation, poor treatment outcomes and High Case Fatality Rate**: A major concern is the delayed diagnosis of prostate cancer cases in Ghana [85% of cases in Ghana report late, compared with what prevails in western countries, where 80% present early for treatment. [Hsing et al, 2000; Globacom Statistics (2020)]. This contributes to the case fatality rate in Ghana that exceeds 50% (Globacon, 2020). Late presentation reduces the likelihood of successful treatment and contributes to the high mortality rate associated with the disease.
2. **Ethno-Demographic Disparities**: Research by Gyedu et al. (2018) has revealed ethno-demographic disparities in prostate cancer. Understanding the impact of ethnicity on disease clustering is essential for tailored interventions and equitable healthcare delivery.
3. **Equity Gaps in Healthcare**: Wide disparities persist in various aspects of prostate cancer care, including policy development, disease awareness, early detection through screening practices, metastasis work-up, and treatment outcomes (Yeboah, 2016; Wiredu et al., 2006; Rawla, 2019). These disparities exacerbate the unequal burden of prostate cancer within the Ghanaian population.
4. **Ineffective Health Promotion**: Existing health promotion efforts are not effectively targeted (Hsing et al., 2000), hindering the dissemination of vital information and preventive measures among at-risk populations.
5. **Accessibility and Cost Barriers**: There are significant challenges related to both physical and financial accessibility to essential medical services. Access to bone scanning, a crucial diagnostic

tool for prostate cancer, is limited (KBTH archives, 2020). Additionally, the cost of screening men for prostate cancer, which stands at $65 USD, is substantially lower than the estimated (at least) $5000 USD required for treatment of advanced disease per-year (Umberto et al., 2017); creating economic disparities in healthcare access.

6. **Biomedical Limitations of PSA**: Prostate-specific antigen (PSA) testing, a primary method for early diagnosis, has imperfections (low specificity, a high false positive rate and a significant false negative rate), raising questions about its effectiveness (globally) and in the Ghanaian context as well (Catalona et al., 2011).

To address these complex challenges and bridge the identified gaps, this study aims to:

- Generate robust statistical evidence on prostate cancer clustering with a specific focus on the impact of demographic characteristics, including ethnicity.
- Develop effective population screening models and disease metastasis prediction tools tailored to the Ghanaian context.
- Promote equitable healthcare policies, awareness campaigns, and early detection practices.
- Enhance accessibility to essential healthcare services, including bone scanning, to improve early diagnosis; by creating technology-driven stratification as alternatives.
- Investigate the limitations of PSA's predictive value; and explore ways of improving that by combining PSA with other determinants in novel models.

By addressing these issues, this study seeks to contribute to reducing prostate cancer morbidity and mortality in Ghana, fostering equitable healthcare delivery, and improving overall public health outcomes of the disease.

1.3 Rationale Of Study

This study anticipates providing crucial insights into the distribution of prostate cancer across Ghana's diverse ethnic and demographic groups. This knowledge will enable more precise targeting of health

promotional efforts; moving away from a one-size-fits-all approach (Odedina et al., 2014). By crafting health messages that consider sociological, demographic, anthropological, and acculturation differences, the chances of success can be heightened. Despite existing studies on ethnic differences in prostate cancer incidence (Biritwum et al., 2016; Gyedu et al., 2018), research focusing on disease risk profiles and treatment outcomes concerning ethnicity remains limited, creating a notable knowledge gap that demands attention.

While prostate cancer is notably prevalent among African-African and African American men (Hsing et al., 2014, Odedina, Ogunbiyi, and Ukoli, 2006), the investigation into potential hereditary links within the Ghanaian population remains unexplored. The presence of heterogeneity in the distribution of prostate cancer cases among Ghana's ethnic groups has not been systematically examined. Addressing this question could shed light on the underlying genetic factors at play, if indeed such heterogeneity exists (Yeboah et al., 2009). This study aims to investigate this aspect by examining potential clusters of prostate cancer occurrence among various ethnic groups in Ghana, among other objectives.

Furthermore, the study's endeavor to develop metastasis prediction tools/models and population screening or prostate cancer disease-detection tools/models for prostate cancer holds promise for economic savings at the level of both the population and health systems. It also has the potential to enhance equity in the prevention, early diagnosis, and treatment of prostate cancer within the Ghanaian population. It also holds promise towards improving geographical and financial accessibility in terms of promptness of determining metastastasis in prostate cancer in Ghana.

In summary, the study on prostate cancer determinants, severity and treatmant outcomes in Ghana could offer substantial public health value across the following critical dimensions:

1. **Tailored Health Promotion**: By grasping ethnic-specific incidence, risk, and treatment dynamics, the study may guide culturally fitting health campaigns for diverse ethnic groups, improving awareness and prevention (Odedina et al., 2014).

2. **Targeted Screening**: Understanding high-risk ethnic groups would enhance focused screening initiatives, aiding early detection and treatment effectiveness (Odedina, Ogunbiyi, & Ukoli, 2006).
3. **Policy Impact**: Findings would influence policy-making for equitable healthcare, fostering targeted interventions, facilities, and management frameworks (McLeroy et al., 1988).
4. **Economic Insights**: By assessing cost-savings potential, the study would efficient resource allocation, alleviating prostate cancer's economic toll (Odedina, Ogunbiyi, & Ukoli, 2006).
5. **Occupation and Environment**: Occupational and environmental links explored could shape policies for vulnerable populations (Hsing et al., 2014).
6. **Effective Project Management**: Evidence directs public health projects, enhancing interventions' precision and impact (Kerry Mckellar, 2020). In essence, the study potentially empowers tailored interventions, policy formulation, and resource allocation for equitable prostate cancer control in Ghana (Wiredu and Armah, 2006; Laryea et al., 2014; Biritwum et al., 2016; Gyedu et al., 2018; Globacon statistics, 2020; Rebbeck et al., 2022).

1.4 Conceptual Framework Diagram

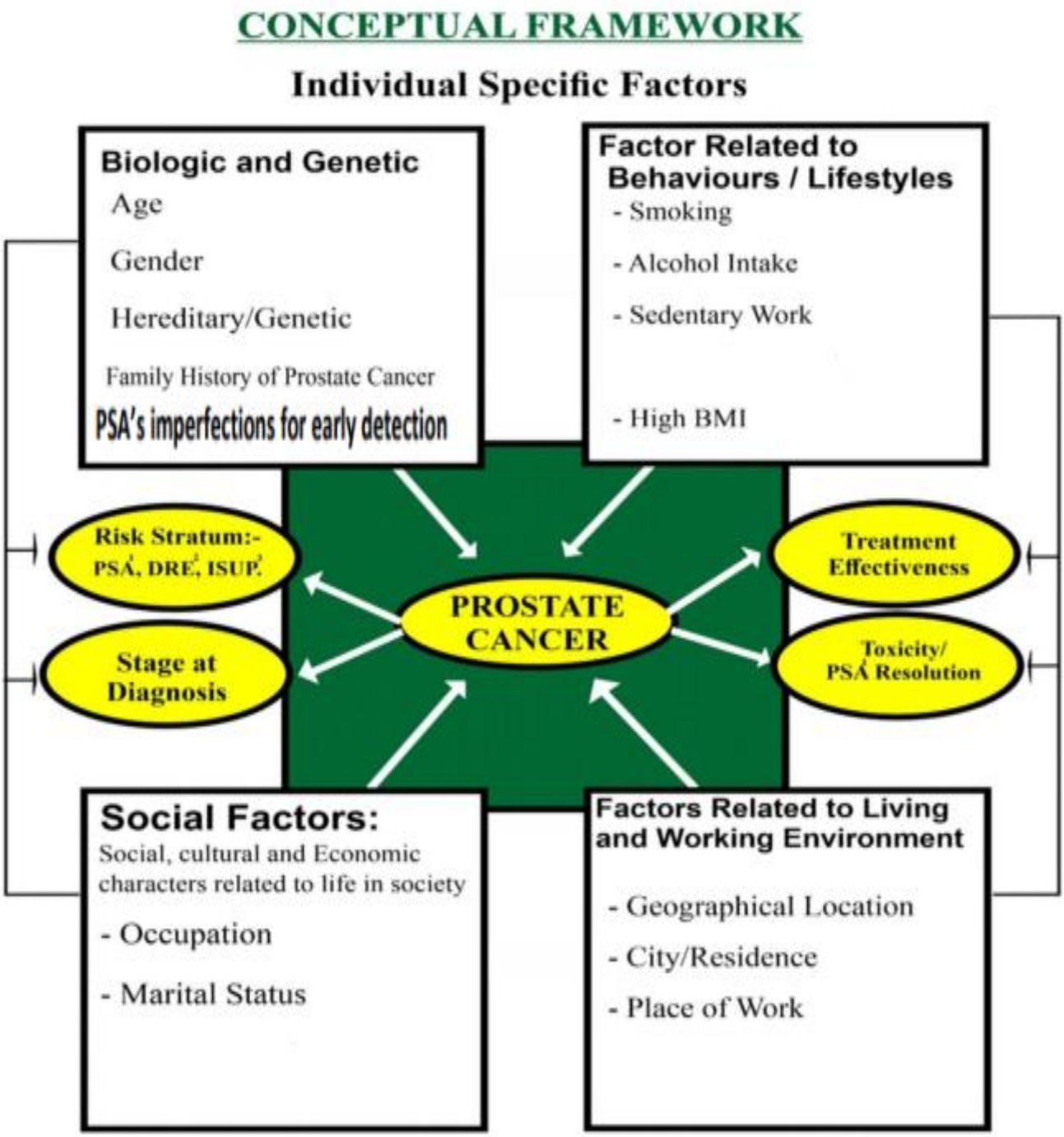


FIG. 1.1: ADAPTED AND MODIFIED FROM THE SOCIO-ECOLOGICAL MODEL (SEM; MCLEROY ET AL., 1988), AND 'THE Amount and various determinants of cancer in Morocco'; Maamri et al., (2015).

PSA[1] = Prostate Specific Antigen; DRE[2] = Stage of disease on Digital Rectal Examination at the clinics; ISUP[3] = International Society of Urologic Pathologists grade of disease on histology.

1.5 Narrative of the conceptual framework

The study's conceptual framework, guided by the Socio-Ecological Model (SEM; [McLeroy et al., 1988]) and Maamri et al.'s work (2015), intricately examines some of Ghana's prostate cancer determinants. This model interconnects individual (genetic/behavioural), interpersonal, and societal aspects, each shaping diverse health outcomes.

Individual factors age, ethnicity and gender, BMI, behaviour/habits, are key to prostate cancer risk. Genetic influences, noted by Rebbeck et al. (2022), particularly within ethnic contexts, play a role. Lifestyle, healthcare access, awareness; and the biomedical problem of PSA's imperfections in early disease detection (Catalona et al., 2011) all influence incidence; and these may affect the disease stage at detection and severity as well. Ultimately, the treatment outcomes, including toxity/risk of side effects get affected in tandemn as well.

Interpersonal dynamics encompass cultural and social forces driving health behavior. Norms, family structures, and support networks (in this study, measured by marital status and occupation/work environment), shape attitudes towards screening and treatment and would influence how early or late a patient presents for treatment; and ultimately, the treatment outcomes. Geographical location, place of work and occupation may all affect geographical accessibility, financial accessibility and therefore treatment effectiveness, in as much as it can affect the health-seeking behaviour (including voluntary screening and uptake of regular health check-ups by individuals); and therefore how early or late the disease is diagnosed. Educational level has similar effects, but this study could not obtain that data from our secondary data source: even though it may largely be alluded from/through the occupations data which we have. However, this study did not analyse directly for educational level. Crucially, the framework highlights core factors: age, ethnicity, occupation, residence, marital status, BMI, alcohol/tobacco use, family history (genetics/hereditary), Prostate Specific Antigen (PSA) levels, and disease stage. While limited by retrospective data, these aspects are captured. In essence, this conceptual framework attempts to unravel

Ghana's prostate cancer complexity, holistically (Wiredu and Armah, 2006; Laryea et al., 2014; Biritwum et al., 2016; Gyedu et al., 2018; Rebbeck et al., 2022).

1.6 Research Questions

1. What are the determinants and trends (demographic, temporal, ethnic-rates-of-disease) of prostate cancer cases presenting at SGMC over the study period?
2. What is the relationship between disease determinants and disease severity(risk category) at diagnosis.
3. What is the relationship between disease determinants and treatment outcomes of the disease?
4. Can we combine PSA, BMI and some of these determinants in a simple model to predict the probability of disease presence (estimated disease-risk level) in an individual?
5. Can BMI (and the other disease determinants) make PSA a better predictor of metastasis in prostate cancer.
6. Can BMI (and the other disease determinants) make PSA a better predictor of treatment outcomes in prostate cancer patients?

1.7 General Objective

The general objective of this study is to investigate prostate cancer disease determinants, severity and treatment outcomes at the Sweden Ghana Medical Center in the Greater Accra Region of Ghana.

1.7.1 Specific Objectives:

1. To assess the determinants and trends (demographic, temporal, ethnic-rates-of-disease) of prostate cancer cases presenting at SGMC over the twelve-year period.
2. To investigate the relationship between disease determinants and disease severity (risk category) at diagnosis.
3. To investigate the relationship between disease determinants and treatment outcomes of the disease.
4. To explore the usefulness of combining PSA and other disease-determinants into simple prostate cancer risk-estimators; with potential for deployment in population screening activities.

5. To examine the usefulness of PSA, BMI (and the other disease determinants) in predicting metastasis in prostate cancer.
6. To examine the usefulness of PSA, BMI (and the other disease determinants) in predicting treatment outcomes, in prostate cancer.

1.8 Profile of Study Area

1.8.1 Country Profile

The Sweden Ghana Medical Centre is located in Accra; in the Greater Accra Region of Ghana.

Ghana is one of the Anglophone countries of the continent Africa, located in the West Africa sub-region, in the sub-Saharan zones. The country is surrounded by Togo, Benin, Nigeria to its Eastern borders; Burkina Faso to the north, La Cote d'Iviore to the west and the Atlantic ocean to the south. Ghana is said to be a low middle-income country (LMIC) with a population of approximately 30.8 million. There are 16 regions in Ghana; with Accra as the capital city of Ghana. Accra is a coastal city of about 5 million populations (Agyekum et al, 2021).

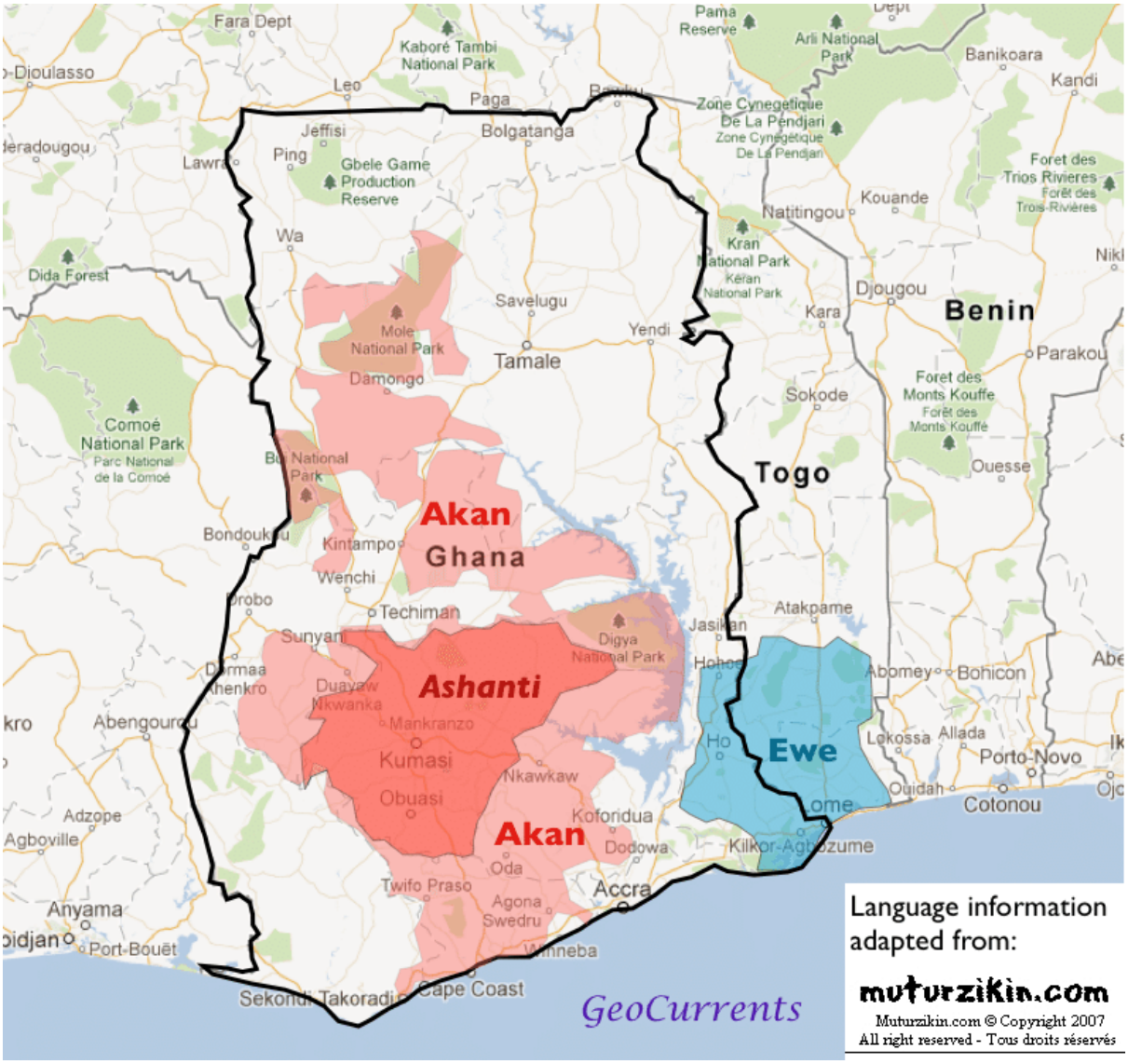


FIG. 1.2: ADAPTED FROM (KOHNERT *ET L.*, 2009)

Ghana is a multi-ethnic sub-Saharan African country. With more than seventy ethnic groups. Major ethnic groups in Ghana include the Akan at 47.5% of the population, the Mole-Dagbon at 16.6%, the Ewe at 13.9%, the Ga-Dangme at 7.4%, the Gurma at 5.7%, the Guan at 3.7%, the Grusi at 2.5%, the Kusaasi at 1.2%, and the Bikpakpaam a.k.a. Konkomba people at 3.5% (2021 Ghana Population and Housing Census).

1.8.2 Profile of the Specific study site

FIG. 1.3: SOURCE, SGMC ARCHIVES, 2023

The Sweden Ghana Medical Centre covers the full range of cancer specialties and utilizes state-of-the art equipment and treatment techniques to provide quality cancer treatment. There are two full-time oncologists who see and treat all the spectrum of cancers, including cancer of the prostate. They also have a lot of supporting staff. The facility has seen over 8000 cancers and managed them since they started operations in 2009. Because of its high quality of service, accessibility and strategic business and marketting activities, the SGMC is not only accessed for care by Ghanaians alone, but by other neighbouring west Africans, and even some few Jamaicans, Caucassians and Asians. The data was collected in this facility.

1.9 Scope of Study

The scope of the thesis titled " Prostate Cancer Disease Determinants, Severity and Treatment Outcomes at The Swedish Ghana Medical Center in the Greater Accra Region of Ghana", bothers on exploring the proportion or case-rates amongst the different ethnicities, factors contributing to the risk of developing the disease, the severity/risk category of the disease at diagnosis and the effectiveness of treatment and other treatment outcomes.

This twelve-year retrospective study explores how determinants influence prostate cancer frequencies, disease characteristics across demographics, and treatment outcomes. It addresses gaps by examining global

and Ghana-specific data, utilizing diverse variables and concepts. The study aims to predictively analyze these dynamics, contributing essential insights into global health.The study delves into various aspects related to prostate cancer:

1. Prostate Cancer trends, disease-determinants and case-frequency Assessment
2. Risk Profile/Disease Severity determinants.
3. Treatment Outcome Evaluation:
4. Predictive modelling to enhance prostate cancer health care.

1.10 Organization of Report

This thesis report is organized into six chapters. Chapter 1 briefly introduces the subject matter of the study, provides a problem statement, justification and states the objectives of the study. In addition, it states and describes the conceptual framework, as well as gives a narration on the study site. Chapter two discusses relevant peer-reviewed literature on the topic of this thesis. In chapter three, the methodology employed in this study, the study design, the analysis of the data and the limitations of the study are discussed. Chapter four summarizes the findings of the study in prose and tables and appropriate figures. In chapter five, the findings of the study are discussed; whilst in chapter six, conclusions; and recommendations are provided for the appropriate bodies they are targeted to. References based on the Harvard referencing style are provided both in-text and at the end of the study report; and an appendix at the tail end of the study provides administrative documents like ethical clearance certificates, letters of introduction and correspondence, and extra tables and charts as well as statistical tests' calculations. At the beginning of the study report, there is a title page; followed with acknowledgements, foreword, a list of abbreviations, table of contents, and a list of abbreviations, figures and tables; as well as a structured abstract; all forming the front-matter, of the thesis report.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1.1 Definition of Terms:

In this literature review on " Prostate Cancer Disease Determinants, Severity and Treatment Outcomes at The Swedish Ghana Medical Centre in The Greater Accra Region of Ghana," the following key terms and their respective definitions are provided for clarity and context:

a. **Prostate Cancer**: Prostate cancer is a malignant tumor that originates in the prostate gland, a small walnut-shaped gland located below the bladder in males. It is the most common cancer in men and is characterized by the abnormal growth of prostate epithelial cells (American Cancer Society, 2021). The predominant (95%) variant of prostate cancer that clinicians and experts routinely/by default refer to as prostate cancer is the adenocarcinoma variant. There are a set of rare variants which form only five percent of all cases; ie small cell, squamous cell, transitional cell, and sarcomas. These may be said to be 'atypical' in nature (and PSA dynamics), and are not the subject matter of this study.

b. **Ethno-Demographic Differences**: Ethno-demographic differences encompass variations in disease prevalence, risk factors, and outcomes among distinct ethnic and demographic groups within a population. These differences stem from genetic, cultural, socio-economic, and geographical influences (World Health Organization, 2019).

Prevalence: In the context of prostate cancer, prevalence signifies the proportion of individuals affected by the disease within a specific population at a given point or over a defined period (National Cancer Institute, 2020). The data we have in this study does not provide us with the numerator to determine prevalence, so we resorted to case frequencies or case rates per each ethno-demographic grouping.

Determinants of disease: for the purposes of this study, the determinants of prostate cancer involves factors that heighten the likelihood of its development. This may include age, family history, genetic predisposition, lifestyle choices, and environmental exposures (Mayo Clinic, 2021).

Risk stratum/category: This measures the severity of the disease as determined by a collection of biologic components inherent to the disease. It pertains to the risk category that prostate cancer falls into, determined by parameters like prostate-specific antigen (PSA) levels, digital rectal examination (DRE) findings, and histological grading (by ISUP).

Outcomes: Prostate cancer outcomes encompass treatment response, disease progression, overall survival, quality of life, and potential complications (American Society of Clinical Oncology, 2018).

Twelve-Year Retrospective Study: A twelve-year retrospective study examines historical data from the past twelve years to explore trends, changes, or associations related to a specific subject, in this instance, prostate cancer in Ghana (National Institutes of Health, 2022).

2.1.2 Reviewed Literature that Align with Index Study Objectives

Objective 1: Assessing Determinants and Trends of Prostate Cancer Cases

In the context of assessing determinants and trends of prostate cancer cases, Hsing et al. (2014) conducted a study in Ghana over a twelve-year period, reporting an alarming increase in prostate cancer cases. Their findings revealed that the incidence of prostate cancer in Ghana had risen from 1,200 cases in 2002 to 2,129 cases in 2014, a significant upward trend. Importantly, they noted that a substantial number of these cases (85%) were diagnosed at advanced stages. According to Umberto et al., 2017; 80% of prostate cases in European countries are diagnosed at early stages, with only 20% being late. The reason behind the disparities, may be the availability of early detection frameworks for prostate cancer that are being strictly implemented; whereas in Ghana, we are relying solely on opportunistic/voluntary screening (Ghana National Cancer Policy, 2017). These findings may have negative effects on our treatment outcomes for prostate cancer in Ghana.

Objective 2: Investigating the Relationship Between Disease Determinants and Disease Severity

Gyedu et al. (2018) focused on ethno-demographic disparities in prostate cancer in Ghana. Their research conducted in Kumasi, Ghana; disclosed that ethnicity played a significant role in disease severity at the time of diagnosis. Specifically, the Akans, showed a higher prevalence of advanced-stage prostate cancer, with figures indicating that over 60% of prostate cancer cases in this group were diagnosed at an advanced stage. This may portend poor prognosis for disease treatment outcomes in our jurisdiction (Wiredu et al. 2006).

Objective 3: Investigating the Relationship Between Disease Determinants and Treatment Outcomes

Wiredu et al. (2006) explored the relationship between disease determinants and treatment outcomes of prostate cancer in Ghana. Their study found that late diagnosis was a prominent factor contributing to poor prognosis. Approximately 70% of patients diagnosed at advanced stages had limited treatment options and experienced poorer outcomes compared to those diagnosed at earlier stages. Comparatively, as observed by Umberto et al., 2017; 80% of prostate cases in European countries are diagnosed at early stages, with only 20% being late. The reason behind the disparities, may be the availability of early detection frameworks for prostate cancer that are being strictly implemented; whereas in Ghana, we are relying solely on opportunistic/voluntary screening (Ghana National Cancer Policy,2012 to 2017).

Objective 4: Exploring Prostate Cancer Risk Estimators for Population Screening

Rawla (2019) conducted a review of studies evaluating various risk factors for prostate cancer. While several studies proposed risk assessment models based on a combination of disease determinants, the congruence of these models with the Ghanaian population remains an area that requires further investigation. The studies reviewed reported risk estimates ranging from 10% to 30% for various risk factors, but specific figures for the Ghanaian context were limited.

Objective 5: Examining the Usefulness of PSA, BMI, and Other Determinants in Predicting Metastasis

Catalona et al. (2011) examined the imperfections of PSA testing in early diagnosis. Their findings suggest that PSA alone may not be a reliable predictor of prostate cancer metastasis, with a sensitivity of around 70% and specificity of approximately 80%. Similar results have been reported in other studies globally (Chun et al., 2007; Shahrokh et al., 2008). The limitations of PSA as a standalone diagnostic tool highlight the need for more comprehensive risk assessment models that incorporate factors such as BMI and other disease determinants specific to the Ghanaian population.

Objective 6: Examining the Usefulness of PSA, BMI, and Other Determinants in Predicting Treatment Outcomes

Umberto et al. (2017) conducted research on the cost-effectiveness of prostate cancer screening and treatment. Their study highlighted the economic disparities associated with treatment costs. They reported that the per- year cost of prostate cancer treatment in Italy averaged around $5,000 USD per patient, while the cost of PSA, clinical assessment and biopsy for screening, together was approximately $65 USD in Ghana. These cost figures underscore the economic challenges associated with prostate cancer treatment in Ghana and emphasize the need for predictive models for treatment outcomes that consider the economic context.

In summary, existing literature that aligns with the objectives of this study, provide specific findings that emphasize the increase in prostate cancer cases, the role of ethnicity in disease severity, and the limitations of PSA testing for screening and metastasis prediction. Further research is warranted to address the unique challenges and opportunities for prostate cancer prevention and management in Ghana while considering these findings.

2.2 Risk Factors and Evidence-Based Prevention of Prostate Cancer

Prostate cancer, a complex disease, is influenced by a range of risk factors established through extensive research. These factors must be considered when developing effective prevention strategies.

Age: Prostate cancer incidence rises significantly after the age of 50 (Rawla et al., 2019).

Family History and Genetics: Having a first-degree male relative with prostate cancer elevates the risk by 1.5 to two-fold (Lichtenstein et al., 2000). Certain genetic mutations, such as BRCA1 and BRCA2, are associated with higher risk (Castro et al., 2015).

Race and Ethnicity: African American men face a heightened risk of prostate cancer and are often diagnosed at advanced stages (Siegel et al., 2016).

Geographic Location: Prostate cancer rates vary by region, with lifestyle and diagnostic efficiency playing a role (Center et al., 2012).

Diet and Lifestyle: High intake of saturated fats and red meat correlates with an elevated risk (Sfanos et al., 2012). Obesity and inactivity increase the risk of aggressive prostate cancer (Discacciati et al., 2011).

Occupational Exposures: Certain work-related chemical exposures, such as cadmium and pesticides, are linked to increased prostate cancer risk (Hayes et al., 1990).

Hormonal Factors: Elevated testosterone levels, especially dihydrotestosterone (DHT), raise the risk (Morgentaler et al., 2006). Low vitamin D levels may also be associated (Schwartz et al., 2005).

Smoking and Alcohol: Smoking heightens aggressive prostate cancer risk, but quitting is beneficial (Kenfield et al, 2011). Excessive alcohol intake might elevate the risk (Bagnardi et al., 2015).

Inflammation and Infections: Prostatitis and potential links to sexually transmitted infections raise questions (Sfanos et al., 2018).

Absence of Medical Check-ups: Late-stage diagnosis due to lack of regular screenings results in poor outcomes (Moyer et al., 2012).

Prevention Strategies:

Diet and Nutrition: A diet rich in fruits and vegetables, reduced red meat, and increased omega-3 fatty acids may lower risk (Giovannucci et al., 2004; Alexander et al., 2010).

Physical Activity: Regular exercise reduces risk (Liu Y. et al., 2016).

Body Weight and Obesity: Maintaining a healthy weight through diet and exercise lowers risk (Discacciati et al., 2011).

Smoking and Alcohol: Avoiding smoking and limiting alcohol intake mitigate risk (Kenfield et al., 2011; Bagnardi et al., 2015).

Regular Medical Check-ups: Early detection through screenings, including PSA testing, improves outcomes (Moyer et al., 2012).

Sexual Activity and Prostate Cancer Risk: Some studies suggest a lower risk with increased ejaculation frequency (Rider et al., 2016). However, factors like sexually transmitted infections may counteract this effect (Sfanos et al., 2018).

Hormonal and Biological Mechanisms: Ejaculation causes temporary hormonal changes, potentially offering protection against prostate cancer (Leitzmann et al., 2004).

Prostate cancer prevention necessitates a holistic approach, considering lifestyle factors, regular check-ups, physical activity and, to some extent, sexual activity.

2.3 Ethno-Demographic Differences in Prostate Cancer Disease, Severity and Treatment Outcomes

2.3.1 Global Overview

Introduction: Prostate cancer's global impact is influenced by diverse ethno-demographic factors. This overview explores how ethnicity, genetics, socio-economics, and environment contribute to disparities in prevalence, risk profiles, and treatment outcomes worldwide.

Prevalence across Ethnic Groups: Prostate cancer's prevalence varies globally among ethnic groups. For instance, African American men have a higher incidence rate compared to men of European or Asian descent, with a lifetime risk of 1 in 7 and 1 in 9, respectively (American Cancer Society, 2021). Some Asian populations exhibit much lower incidence rates (Zhou et al., 2017).

Genetic Factors and Ancestry: Genetic variations play a significant role in prostate cancer risk among different ethnicities. BRCA1 and BRCA2 mutations are associated with higher risks, especially among Ashkenazi Jews (Leongamornlert et al., 2012).

Socio-Economic and Environmental Influences: Socio-economic factors and environmental exposures contribute to disparities. Limited access to healthcare, dietary patterns, and carcinogen exposure impact disease risk (Pernar et al., 2016).

Risk-Stratification Profiles: Different ethnic groups show varying risk profiles, influencing treatment and outcomes. African American men may present advanced-stage disease and have higher recurrence risks (Vance et al., 2015).

Treatment Disparities and Outcomes: Disparities in treatment and outcomes exist globally due to variations in healthcare systems, treatment options, and patient preferences (Magheli et al., 2018).

Conclusion: Ethno-demographic nuances significantly influence prostate cancer's prevalence, risk profiles, and outcomes worldwide. Customized strategies, collaborative efforts, and culturally sensitive healthcare approaches are essential for equitable prostate cancer care.

2.3.2 African Overview

Introduction: Prostate cancer's significance in Africa varies among countries and ethnic groups.

Prostate Cancer Burden in Africa: Prostate cancer is prevalent in Africa, with a significant impact. In sub-Saharan Africa, an estimated 61,978 new cases and 36,292 deaths occurred in 2020 (Global Cancer Observatory, 2020). Prostate cancer comprises about 14% of all cancer cases and 8.2% of cancer deaths in African men (Global Cancer Observatory, 2020).

Ethnic and Regional Variations: Differences in prostate cancer prevalence emerge within African ethnic groups. For example, in Nigeria, the Igbo ethnic group has a higher incidence than the Yoruba group (Odedina et al., 2009). Men of African ancestry often experience more aggressive prostate cancer forms (Jemal et al., 2016).

Genetic Factors and Ancestry: Genetic factors play a role in African prostate cancer risk. Specific variants, like single nucleotide polymorphisms (SNPs), link to higher risk. HNF1B gene SNPs correlate with African American men's prostate cancer risk (Han et al., 2016).

Barriers to Early Detection and Treatment: Challenges hinder early detection and treatment in Africa, including limited healthcare access and low awareness, delaying diagnoses (Ekwueme et al., 2015).

Treatment Disparities and Outcomes: African nations witness treatment disparities due to healthcare infrastructure and cultural influences, impacting treatment choices.

Collaborative Efforts and Awareness: Collaboration between local and international entities, governments, and healthcare institutions aims to reduce disparities. Awareness campaigns and outreach initiatives enhance early detection and treatment access.

Conclusion: Ethno-demographic disparities profoundly impact prostate cancer in Africa. Customized interventions, awareness campaigns, and sensitive healthcare approaches are essential to address these challenges and achieve better prostate cancer outcomes across the continent.

2.4. Prostate Cancer in Ghana: An Ethno-Demographic Perspective

Introduction: Prostate cancer poses a significant health challenge in Ghana. Understanding ethno-demographic variations in its prevalence, risk profiles, and treatment outcomes is essential for effective management and public health planning. This section reviews the Ghanaian literature on prostate cancer, examining the impact of factors such as ethnicity, socio-economic status, and healthcare access on disease burden and treatment outcomes among Ghanaian men.

Prostate Cancer Burden in Ghana: Prostate cancer is the most common cancer among Ghanaian men in terms of incidence and mortality, with a steadily rising trend. In 2020, it accounted for 16.9% of all cancer cases in men (Ghana Cancer Registry, 2020). Ghana's high case fatality rate of around 50.0% is primarily due to low cancer awareness and late-stage presentations (Globacom Statistics, 2020). Targeted interventions are needed to improve outcomes.

Ethnic and Regional Variations: Studies in Ghana have reported variations in prostate cancer incidence among ethnic groups and regions. For example, the Ashanti region has a higher prevalence than other regions, and men of Akan ethnicity face a higher risk (Biritwum et al., 2016; Gyedu et al., 2018).

Barriers to Early Detection and Treatment: Ghana faces challenges in early detection and treatment, including limited healthcare access, low awareness of screening, and cultural beliefs contributing to delayed diagnoses. Educational campaigns targeting Ghanaian men's awareness of prostate cancer are needed (Glover et al., 2017).

Treatment Disparities and Outcomes: Treatment disparities exist in Ghana due to variations in access and patient preferences. Geographic location plays a role, with access to comprehensive cancer centers impacting treatment options and outcomes (Ansong et al., 2020).

Collaborative Efforts and Awareness Campaigns: Addressing prostate cancer disparities in Ghana involves collaborations between the government, NGOs (non-governmental organizations), and healthcare

institutions. Awareness campaigns and public health initiatives aim to improve early detection, treatment access, and overall outcomes.

Conclusion: The existing body of literature on prostate cancer in Ghana, reveals ethno-demographic differences in disease burden, risk profiles, and treatment outcomes. Understanding these variations is crucial for implementing targeted interventions, improving early diagnosis, and ensuring equitable access to quality care. Collaborative efforts, research, and culturally sensitive healthcare approaches are essential for reducing the burden of prostate cancer among Ghanaian men.

2.5 Behavior Change Strategies in Prostate Cancer Prevention:

Introduction: Prostate cancer's impact in Ghana necessitates effective health promotion strategies and policies to enhance screening rates and early diagnosis. This section outlines evidence-based approaches, incorporating behavior change theories, tailored to Ghana's ethno-demographic context.

1. **Community-Based Education and Awareness Programs**: Implementing community-centric education programs is crucial for raising awareness and facilitating early detection. Culturally relevant messages, collaboration with local leaders, and health workers enhance program credibility and reach (The World Bank, 2019).
2. **Social Cognitive Theory**: Applying the Social Cognitive Theory encourages screening and preventive behaviors. Positive role models and promotion of early detection benefits boost men's confidence (Bandura, 2006).
3. **Leveraging Technology: Mobile Health (mHealth) Interventions**: mHealth tools like text messages and mobile apps transcend geographical barriers and improve health information dissemination. Tailoring messages and sending screening reminders ensures better adherence (The World Bank, 2019).

4. **Culturally Sensitive Communication**: Effective communication requires cultural relevance. Customized materials reflecting norms and values enhance understanding and acceptance (Kreuter et al., 2003).
5. **Community Screening Camps**: Organizing community screening camps enhances accessibility, particularly in underserved areas. Collaboration with local health facilities and organizations builds trust and participation, bridging ethnic disparities (The World Bank, 2019).
6. **Socio-Economic Empowerment**: Integrating prostate cancer services into primary healthcare addresses socio-economic gaps. Ensuring affordability and access for all socio-economic strata improves early diagnosis and reduces inequities (Gyedu et al., 2018).

Conclusion: Tailored health promotion and policies in prostate cancer care are needed to reach-out to all Ghana's ethno-demographic variations. Employing community-based education, behavior theories, mHealth, cultural sensitivity, community engagement/co-creational approaches (Boateng M. et al., 2021), can elevate screening rates and early diagnosis, reducing the burden of prostate cancer across diverse populations. Health equity remains fundamental, towards promoting better health and well-being for all (Cohen et al., 2017; Haynes et al., 2015; Redwood et al., 2014).

2. 6 Causation as a Principle of Epidemiology as applied to Prostate Cancer Disease

Causation in prostate cancer epidemiology involves examining risk factors' connections with disease outcomes. Risk factors can be categorized by necessity and sufficiency, and in brief, are as follows:

1. Age: Advanced age is necessary but not sufficient for prostate cancer (Ezioni et al., 2002).
2. Family History: Family history is necessary and sometimes sufficient (Siegel et al., 2021).
3. Genetic Factors: Can be both necessary and sufficient (Cuzick et al., 2014).
4. Lifestyle Factors: Not necessary but sometimes sufficient (Siegel et al., 2021).
5. Occupational Exposures: Sometimes necessary, not sufficient alone (Ezioni et al., 2002).
6. Smoking: Neither necessary nor sufficient (Ezioni et al., 2002).

7. Alcohol Consumption: Neither necessary nor sufficient (Siegel et al., 2021).
8. High BMI/Obesity: A risk factor but not necessary or sufficient alone (Ezioni et al., 2002).
9. Ethnicity: Complex, neither necessary nor sufficient alone (Siegel et al., 2021). Some other researchers also argue that ethnicity is necessary for some groups, but not sufficient alone (Ziegler-Johnson et al., 2017).

Prostate cancer causation is multifactorial, involving risk factors' interactions. A comprehensive understanding helps in prevention and care, especially in specific ethnic populations (Cuzick et al., 2014).

2.7 Ethnic Diversity in Ghana and Prostate Cancer Risk

Introduction: Ghana is a diverse country with numerous ethnic groups, each contributing to its cultural richness. Understanding this diversity is crucial for tailoring effective prostate cancer health initiatives and considering genetics in disease risk. This section provides an overview of major ethnic groups in Ghana and explores the role of genetics in prostate cancer risk across different populations.

2.7.1 Ethnic Diversity in Ghana:

Ghana hosts several major ethnic groups, each with distinct histories and cultural practices. The largest ethnic groups, along with their population percentages, are:

1. **Akan**: Representing about 47.5% of the population, the Akan group includes subgroups like the Ashanti and Fante.
2. **Mole-Dagbon**: Comprising roughly 16.6% of Ghanaians, they mainly reside in the Northern Region.
3. **Ewe**: About 13.9% of the population, primarily found in the Volta Region.
4. **Ga-Dangme**: Representing approximately 7.4% and concentrated in the Greater Accra Region.
5. **Gurma**: Accounting for around 5.7% and primarily located in the Upper East Region.

Understanding these diverse ethnic groups is vital for developing culturally sensitive health initiatives, including those related to prostate cancer.

2.7.2 Genetics and Prostate Cancer Risk in general:

Genetic factors significantly impact prostate cancer susceptibility, with variations observed among ethnic groups globally. Specific genetic markers, such as (single nucleotide polymorphisms) SNPs in BRCA1, BRCA2, and HOXB13 genes, are associated with prostate cancer risk (Chen et al., 2015; Pomerantz et al., 2010).

2.7.3 Ethnicity and Prostate Cancer Risk in Ghana:

While genetic research within specific Ghanaian ethnic groups is limited, studies from similar African populations have shown variations in genetic susceptibility to prostate cancer. Men of African descent, exhibit a higher risk of aggressive prostate cancer compared to men of European or Asian ancestry (Tan et al., 2000).

In their research related to the Cytochrome P4501B1 (CYP1B1) gene's involvement in the activation of various carcinogens and the metabolism of steroid hormones, including 17β-oestradiol (E2) and testosterone, Tan et al., 2000 reported notable differences in the allele frequencies of two point mutations found in the coding region of the CYP1B1 gene across three distinct populations: Caucasian (n = 189), African-American (n = 52), and Chinese (Linxian; n = 109).

Tan et al., 2000, observed that a specific A (C to G) transversion at position 1666 in exon 3, leading to an amino acid substitution from Leu432 to Val, exhibited varying prevalence across ethnic groups. In African-Americans, the allele frequency for Val432 was notably higher at 0.75, while in Caucasians, it was 0.43, and in the Chinese population, it was 0.17. Furthermore, another A (C to T) transition at position 1719 in exon 3, resulting in no amino acid change (Asp449), appeared to be closely associated with the Val432 variant.

Tan et al., 2000 also conducted experiments using human lung microsomal preparations from individuals with different CYP1B1 genotypes, including CYP1B1Val/Val and CYP1B1Leu/Leu. Their results indicated that the Val432 variant may represent a high activity allele, potentially contributing to inter-individual

variations in CYP1B1 enzyme activity. Given CYP1B1's role in hormone and carcinogen metabolism and considering the varying rates of prostate cancer among different ethnic groups, the study also explored the potential association of the CYP1B1 Leu432Val polymorphism with prostate cancer risk in a pilot case–control study.

Among Caucasians, the preliminary findings suggested that 34% of men with prostate cancer (n = 50) were homozygous for the Val432 polymorphism, whereas only 12% of the matched control subjects (n = 50) exhibited this genotype. These initial results indicate that genetic polymorphisms in CYP1B1 may play a significant role in the development of prostate cancer in the Caucasian population (Tan et al., 2000).

Implications for Healthcare: Understanding genetic influences on prostate cancer among different ethnic groups has healthcare implications. Personalized screening and prevention strategies can be developed based on individual genetic risk profiles, considering Ghana's diverse genetic landscape. Integrating genetic testing into routine healthcare can enhance risk assessment and early detection efforts (Kote-Jarai et al., 2013).

Conclusion: Ghana's ethnic diversity calls for individualized approaches to prostate cancer prevention and management. While specific genetic data within Ghanaian ethnic groups are limited, recognizing genetic variations among different populations is vital for addressing prostate cancer disparities and tailoring effective healthcare strategies based on unique genetic makeup.

2.7.4 Core Principles of Prostate Cancer Screening:

1. **Early Detection:** Screening aims to identify prostate cancer at an early, more treatable stage (Heidenreich et al., 2018; Hugosson et al., 2019).
2. **Risk Assessment:** Consider individual risk factors, such as age, family history, and ethnicity, when deciding who should be screened (National Comprehensive Cancer Network, 2021).
3. **Informed Decision-Making:** Encourage shared decision-making between healthcare providers and patients, providing information about benefits and potential harms (American Cancer Society, 2020).

4. **Regular Monitoring:** Implement screening protocols tailored to individual risk profiles, considering both PSA testing and digital rectal examination and then prostate core biopsy for histological diagnosis, when indicated (Mottet et al., 2017).

2.8 Prostate Cancer Diagnosis: Clinical, Imaging and Staging Investigations

Introduction:

Timely and accurate prostate cancer diagnosis improves patient outcomes. Combining medical history, exams, biopsies, and imaging techniques enhances detection and staging. Diagnostic methods include:

1. History and Physical Exam: Patient history and Digital Rectal Examination (DRE) guide diagnosis, although DRE may miss early-stage cases (American Urological Association, 2021).
2. Transrectal Ultrasound (TRUS) and Biopsy: TRUS visualizes the prostate and guides biopsy for histopathological analysis. Biopsy confirms cancer presence and assesses aggressiveness (National Comprehensive Cancer Network, 2021).
3. Advanced Imaging: a. Abdomenopelvic Ultrasonography (USG): High-resolution ultrasonography assesses the prostate and stages disease, detecting liver nodules/metastasis. b. Chest X-ray (CXR): Rules out lung metastasis. c. Technetium Bone Scan: Detects bone metastases (National Comprehensive Cancer Network, 2021). d. Pelvic and Whole Body Diffusion MRI: Sensitive MRI technique assesses the prostate, extracapsular extension, lymph node involvement, and distant metastases.

Conclusion: Prostate cancer diagnosis integrates history, physical examination, and advanced imaging. TRUS biopsy confirms the diagnosis, and as well, establishes the gleason score/ISUP grade. In addition, the USG, CXR, Technetium bone scan, and MRI help establish the disease stage; so that treatment can be comprehensively tailored to the individual and disease to improve outcomes of treatment/management of disease (National Comprehensive Cancer Network, 2021).

2.9 Prostate Cancer Staging on DRE:

Introduction:

Digital Rectal Examination (DRE) is a crucial component of the diagnostic evaluation for prostate cancer. It allows healthcare providers to assess the prostate gland's size, texture, and any palpable abnormalities, providing valuable information for staging the disease.

Staging on DRE:

During DRE, the physician inserts a gloved, lubricated finger into the rectum to palpate the prostate gland. Staging on DRE involves evaluating the extent of the tumor within the prostate and its potential spread beyond the gland's confines. The findings on DRE are classified into the following stages based on the TNM (Tumor, Node, Metastasis) system:

1. Stage T1: The tumor is not palpable and is only incidentally detectable after histology for a trans-rectal resection of the prostate for a benign disease; or through imaging (multiparametric MRI) and biopsy necesitated in a patient due to a persistently elevated PSA.
2. Stage T2: The tumor is confined within the prostate gland and is palpable on DRE.
3. Stage T3: The tumor extends beyond the prostate capsule, involving the seminal vesicles.
4. Stage T4: The tumor has invaded adjacent structures, such as the bladder or rectum (National Comprehensive Cancer Network, 2021).

2.10: Summary of Tailored Management of Prostate Cancer and Iatrogenesis; (please see details of this section in appendix 2 of this thesis document)

Prostate cancer is staged using the TNM system, evaluating the tumor's extent (T), lymph node involvement (N), and distant metastasis (M) (National Comprehensive Cancer Network, 2021). Localized disease (T1-T2, N0, M0) remains confined to the prostate. Locally advanced disease (T3-T4, N0, M0) extends beyond the prostate but not to distant sites. Metastatic disease (M1a, M1b, M1c) spreads to non-regional lymph nodes, bone, or distant organs (Kyei et al., 2012), guiding treatment decisions.

Prostate-specific antigen (PSA) stratification further categorizes localized disease into low-risk (PSA < 10 ng/mL), intermediate-risk (PSA 10-20 ng/mL), and high-risk (PSA > 20 ng/mL) groups, aiding treatment planning (National Comprehensive Cancer Network, 2021).

Histological grades, assessed by Gleason scores/ISUP grades, indicate cancer aggressiveness. Gleason scores combine primary and secondary patterns, while ISUP simplifies grading into five categories (Epstein et al., 2016). Based on ISUP, PSA and DRE findings, the disease can be risk stratified. ISUP 1 is low-risk; ISUP 2-3 is intermediate-risk, and ISUP 4-5 is high-risk for localized disease.

Overall risk stratification of prostate cancer (D'Amico Classification); combines PSA, DRE, and ISUP risk groups (Mohler et al., 2020). Patients can be categorized as low, intermediate, or high risk, guiding treatment selection.

Prostate cancer treatments include active surveillance, surgery, radiation therapy, androgen deprivation therapy, chemotherapy, targeted therapy, and immunotherapy (Akpinar et al., 2017; Alexander et al., 2010). Multimodal approaches may be used for high-risk cases.

Treatment outcomes are monitored through PSA response, tumor control, side effects, and overall survival. Patient-specific treatment plans aim to balance disease control and quality of life.

Iatrogenic harm and toxicities vary by treatment modality. Surgery may lead to infections, incontinence, and erectile dysfunction (Akpinar et al., 2017). Radiation can cause fatigue, skin irritation, and long-term urinary and bowel issues (Mottet et al., 2017). ADT may result in osteoporosis, hot flashes, and mood changes (Shahinian et al., 2005). Chemotherapy and targeted therapy have side effects like nausea and fatigue, while immunotherapy can trigger autoimmune reactions (Michot et al., 2016).

High-quality care involves close patient monitoring, early detection, and comprehensive education to manage treatment-related challenges effectively.

CHAPTER 3

3.0 METHODOLOGY

3.1 Research Methods and Design (Study methods and design)

This is a twelve-year analytical study, involoving an analysis of secondary data from the electronic archives of SGMC, Accra. It is census study, completely enumerating all patients who have assessed the facility for care for prostate cancer of all stages. It is an analytical study, and it adopted a quantitative approach.

3.2 Data Collection Techniques and Tools

An Ms Excel spreadsheet with all the needed parameters was used for the data collection in this study. It is in a separate document, and is inserted at the appendix of this document. The check-list had three sections: section 1 deals with demographic data; section 2 collects data on clinical parameters (smoking and alcohol habit were also included here); and section 3 collects data on family history of prostate, breast and bladder cancer or any other notable cancer present in the family.

3.3 Study Population

All patients who presented to SGMC for prostate cancer care between 20th March 2011 to 19th March 2023; who fit into the inclusion and exclusion criteria of this study were studied.

3.4 Inclusion Criteria

All patients with a positive histopathology result and on treatment for prostate adenocarcinoma, irrespective of the stage.

3.5 Exclusion Criteria

Patients with the other ‘atypical’ or ‘unusual’ or rather rare variants of prostate cancer (small cell, transition cell, squamous cell carcinoma, neuro-endocrine cell carcinoma, prostate sarcoma etc. which, together, constitute only five percent of all cases of prostate cancer) or secondaries; that also affect the prostate gland.

3.6 Study Variables

INDEPENDENT VARIABLES include Age, Ethnicity, Occupation, Marital Status, BMI, Alcohol Use, Tobacco Use, Family History of Prostate Cancer, Previous medical History /Presence of Co-Morbidities.

1. **Age:** The chronological age of the individual, a key factor in understanding health risks and susceptibility to diseases like prostate cancer.
2. **Ethnicity:** The cultural and ancestral background of an individual, which can influence genetic predisposition and disease risk, including prostate cancer.
3. **Occupation:** The type of work or job an individual is engaged in, which may expose them to certain environmental factors that could impact health, including prostate cancer risk.
4. **Marital Status:** The marital condition of an individual (e.g., married, single, divorced), which can have social and psychological effects that might influence health behaviors and outcomes.
5. **BMI (Body Mass Index):** A numerical measure derived from a person's weight and height, providing insight into their body composition and potential risk for health conditions, including prostate cancer.
6. **Alcohol Use:** The consumption of alcoholic beverages, which can impact health, including prostate cancer risk, if consumed excessively.
7. **Tobacco Use:** The use of tobacco products, particularly smoking, which is a well-known risk factor for various cancers, including prostate cancer.
8. **Family History of Prostate Cancer:** The presence of a history of prostate cancer among close relatives, which can indicate a genetic predisposition to the disease.
9. **Previous Medical History / Presence of Co-Morbidities:** A person's past medical conditions or existing health issues (hypertension, diabetes, obesity, heart disease), which could influence their overall health status and interact with prostate cancer outcomes.

These independent variables collectively provide valuable information on the determinants of prostate cancer disease in the individuals in the study population. These may also affect the severity of the disease at diagnosis; and thus the disease treatment outcomes.

DEPENDENT VARIABLES include DRE Stage at Diagnosis, PSA at Diagnosis, Highest PSA, ISUP GRADE, Risk Category/Stratum, Metastasis or No Metastasis, Site of Metastasis, Treatment Intent, Treatment Type, Curative Radiation Treatment Planned, Dose of Radiation Treatment Received (in Grays), Hormonal Therapy. The final set, and true dependent variables include PSA Post-Treatment/ Lowest PSA, PSA Resolution, PSA Resolution per-Gray of Radiation Dose Received, PSA Resolution per Number Of Treatment Modalities Received Per Patient, Fail PSA, Type of Adjuvant Therapy given and Toxicity. ***An important factor to note here is that; these variables are dependent variables up to the time that we are assessing disease severity and the type of treatment modalities to be given to the patient. Beyond this level, they all also become independent variables that could predict treatment outcomes as well. This makes the variables in this study not straightforward to categorise. The categorization relies on domain knowledge of the field of Urology.***

The details of the above variables are as follows:-

1. **DRE Stage at Diagnosis:** Digital Rectal Examination Stage at Diagnosis. This refers to the stage of prostate cancer determined through Digital Rectal Examination (DRE), which assesses the size, shape, and consistency of the prostate gland and checks for abnormalities.
2. **PSA at Diagnosis:** Prostate-Specific Antigen at Diagnosis. PSA stands for Prostate-Specific Antigen, a protein produced by the prostate. PSA levels in the blood can indicate prostate health, with higher levels potentially indicating prostate issues like cancer.
3. **Highest PSA:** The highest recorded Prostate-Specific Antigen level during the course of monitoring and treatment.

4. **ISUP GRADE:** International Society of Urological Pathology Grade. The ISUP Grade classifies the cellular characteristics of prostate cancer to better understand its behavior and potential outcomes. It is gleaned from the histological Gleason Scores.
5. **Risk Category/Stratum:** Categorization of the risk level of prostate cancer, often determined by considering PSA, Gleason Score, and clinical stage.
6. **Metastasis or No Metastasis:** Indicates whether the cancer has spread to other parts of the body (metastasis) or not.
7. **Treatment Type:** The specific approach used to treat prostate cancer, which can include surgery, radiation, chemotherapy, hormone therapy, etc.
8. **Dose of Radiation Treatment Received (in Grays):** The measurement of radiation received during treatment, typically in Grays (Gy).
9. **Hormonal Therapy:** Treatment involving medications that block or reduce the effects of hormones like testosterone, which can fuel prostate cancer growth.
10. **PSA Post-Treatment/Lowest PSA:** The Prostate-Specific Antigen level after completing treatment, often indicating treatment effectiveness.
11. **PSA Resolution:** Reduction of Prostate-Specific Antigen levels post-treatment.
12. **PSA Resolution per-Gray of Radiation Dose Received:** How much Prostate-Specific Antigen levels drop per unit of radiation dose.
13. **PSA Resolution per Number Of Treatment Modalities Received Per Patient:** How Prostate-Specific Antigen levels drop based on/per the number of different treatment approaches.
14. **Fail PSA:** Prostate-Specific Antigen levels that do not decrease as expected post-treatment.
15. **Type of Adjuvant Therapy Given:** Additional treatment given after the primary treatment to enhance its effectiveness.
16. **Toxicity:** Adverse effects or harm caused by treatment, often assessed by monitoring side effects.

These dependent variables collectively provide important information about the diagnosis, treatment, and outcomes of prostate cancer patients. The various PSA parameters, together seek to investigate, analyse and

find out models that could address the biomedical/epidemiological imperfections of PSA, as a biomarker for prostate cancer, within the context of this study.

3.7 Sampling Technique

This is a census study, so a complete enumeration of all patients seen at the facility for prostate cancer during the study period who fit the exclusion and inclusion criteria of this study were included.

3.8 Calculation of Sample Size

This is a census study, so there was no need to calculate a sample size

3.9 Pretesting

There was no need pretesting as the study employed the use of secondary data.

3.10 Data Handling

Permission and administrative clearance was obtained from the management and clinicians of the SGMC from which the secondary data was collected.

Data represent the privacy of patients and the facilities concerned, which are sacrosanct. The data obtained was de-identified and guarded carefully, with soft copies of data saved on a password-protected laptop; and any hardcopy kept under lock and key. The names of the facility concerned shall not be spelt – out in any publications made. All the ethical principles for research were observed, strictly.

3.12 Statistical (Data) Analysis

Data obtained was cleaned in Ms Excel software, and the cleaned data imported into STATA statistical software package (*StataCorp.2007. Stata Statistical Software. Release 17. StataCorp LP, College Station, TX, USA*) for analysis.

Tables and graphs were used to summarise the data, and descriptive statistics (frequencies, mean, median, mode, range, quartiles, standard deviation) were used to summarise numeric data further. Chi – square analysis and Fischer – test were used used to decipher the relationship between/amongst categorical data. Univariate or multivariate analysis were used to study the association between numeric data. All analysis

was done at an alpha of 0.05, and a 95% confidence level; to determine statistical significance. The analysed data was aggregated into information that would be synthesized and discussed and used to influence public policy and public and clinical healthcare practices. Regression analysis for patient age at presentation, ethnic group, (disease-risk profile) based on; Gleason score/the international society for urologic pathology (ISUP) grade of the disease, disease stage at presentation; and prostate-specific antigen (PSA) levels at presentation and other demographic characteristics, was done against disease treatment outcomes measured by PSA resolution-per number of radiation cycles/unimodal or multi-modal treatment approaches, cure or relapse or treatment failure.

3.13 The Analysis and Coding Process

Variables and Coding Plan: A. Independent Variables:

1. **Age and Age-Categories:** Age was coded numerically. Age-categories were created, such as <45 (1), 45 to 54 (2), 55 to 64 (3), .65 to 74 (4), 75 to 84 (5). 85+ (6).
2. **Ethnicity:** Four major groups coded as Akan (1), Ga (2), Ewe (3), and Northern (4). This was limited to 4 only, for Ghanaians due to the quality of data we had. Additional codes for Other West African (5), Other Non-West African African (6), and European/Asian/American (7).
3. **Occupation and Marital Status:** Coded as Sedentary (1), Manual (2), Sporting (3), and Marital status as Single (0) or Married (1).
4. **BMI and BMI Categories:** BMI calculated and coded. Categories: Underweight (1), Normal (2), Overweight (3), Obese/Morbidly Obese (4-6).
5. **Alcohol Use, Tobacco Use, Family History, and Co-morbidities:** Coded as Yes (1) or No (0).
6. **Geographical Location and Nationality:** Location coded as Urban (1), Periurban (2), Rural (3). Nationality encompassing different groups.

B. Dependent Variables:

1. **DRE Stage at Diagnosis:**

T1 to T2C = Localised Disease (coded as 1)

T3A, T3B , T4 WITH NO METASTASIS =Locally Advanced Disease (coded as 2)

ANY T STAGE WITH METASTASIS ANYWHERE = Advanced/Metastatic Disease. (coded as 3)

2. **DRE T-STAGE RISK Categories:** Stages coded and categorized: T1-T2A =Low risk (1); T2B AND T2C; = Intermediate risk (2),

   T3 and T4 = high risk (3)

3. **PSA at Diagnosis:** Coded as continuous numerical variable.
4. **PSA at Diagnosis, categories: Low risk:** PSA < 4 ng/Ml; given that it is localised disease (1), **Intermediate risk:** PSA 4 - 10 ng/Ml; given that it is localised disease (2), **High risk:** PSA > 10 ng/Ml; given that it is localised disease (3)
5. **Gleason Sum Score and ISUP Grade:** Gleason Score was converted to ISUP grades 1, 2, 3, 4, and 5; and coded categorically, as follows: -

   ISUP 1; given that it is localised disease = Low-Risk (1):

   ISUP 2 and 3; given that it is localised disease = Intermediate-Risk (2),

   ISUP 4 and 5; given that it is localised disease = High-Risk (3).

6. **OVERALL RISK CATEGORY:**

   Overall Low-Risk: for those with only low risk for all three parameters; PSA Low + DRE Stage 1-2 + ISUP Grade 1 (1)

   Overal Intermediate-Risk: all three parameters, PSA, DRE, ISUP Intermediate risk; or two intermediate risk in the presence of one low risk, or one intermediate risk in the presence of two low risk (2)

High-Risk: once any one of the parameters PSA, DRE or ISUP puts the patient at high risk level, it is an overall high risk category; coded as (3) in the analysis.

7. **Metastasis:** Coded as binary: Yes (1) or No (0).
8. **Site of Metastasis:** Coded based on locations. Lymph nodes (1) Bone (2), Lungs (3), Liver (4), Other (5).
9. **Hormonal Therapy:**

   Hormonal therapy were coded as binary:

   1. Yes (1)
   2. No (0)

10. **PSA Post-Treatment (Lowest PSA/NADIR) and PSA Resolution:**
    1. PSA post-treatment were kept as a continuous numerical variable.
    2. PSA resolution were calculated (PSA AT DIAGNOSIS MINUS, PSA POST – TREATMENT) and retained as a continuous numerical variable.
11. **PSA Resolution Categories and PSA Resolution per Gray:**
    1. PSA resolution categories were coded based on specific ranges.
    2. PSA resolution per Gray were calculated (PSA resolution divided by Grays given) and retained as a continuous numerical variable.
12. **PSA Resolution per Number of Treatment Modalities:**
    1. PSA resolution per number of treatment modalities were calculated (PSA resolution divided by number of treatment modalities administered) and retained as a continuous numerical variable.
13. **Fail PSA and Fail PSA Categories:**
    1. Fail PSA were kept as a continuous numerical variable.
    2. Fail PSA categories were coded based on specified ranges.
14. **Fail PSA as multiples of Nadir PSA, Adjuvant Therapy, Toxicity:**

1. Fail PSA as multiples of Nadir PSA (fail PSA divided by Nadir) were calculated and retained as a continuous numerical variable. It was further categorised into four classes with codes.
2. Adjuvant therapy was coded as
    1. Yes (1)
    2. No (0)

15. **Highest PSA during treatment course:** Coded as continuous numerical variable; and also categorised.
16. **Treatment Variables:** Type coded based on approaches. Radiation dosage, hormonal therapy, adjuvant therapy coded.
17. **Toxicity:** Coded as binary: Yes (1) or No (0).

C. Analysis Approach:

1. **Descriptive Statistics:** we calculated descriptive statistics for coded variables.
2. **Associations and Relationships:** we explored associations using Chi-square, Fischer-tests, univariate, and multivariate regression analyses.
3. **Mathematical Models:** Mathematical models linked to determinant variables were developed for predictive accuracy. The mathematical models were developed through backwards stepwise-logistic regression analysis with iterations; post-fit tests, discriminant analysis and sensitivity analysis.

3.14 Controlling for Confounders in this Retrospective Study

Managing confounders is vital in retrospective studies using secondary data to ensure accurate results (Smith et al., 2020). Confounders, which are variables associated with both the independent exposure and dependent outcome, can distort their relationship. In our study, we attempted a meticulous approach as follows:

1. **Identifying Potential Confounders**: Comprehensive literature review and data analysis preceded the study to help identify potential confounders. (we followed Jones and Williams, 2018, on this and did a good literature review; which made us wish for controls and educational level, diet habits, exercise habits and quantity of smoking and alchol consumption volumes data; which were not available to us).
2. **Comprehensive Data Collection**: attempts to obtain as much data as possible; were made, to help us possibly gather data on some confounders that may not be too obvious to us from the outset (Thompson et al., 2017). We were limited in this because our data was secondary, but we made efforts to dig into all archives to get as much as we could.
3. **Adjustment Techniques**: appropriate statistical methods like multivariable regression analysis were utilised, to control for confounding (VanderWeele and Ding, 2017).
4. **Sensitivity Analyses**: sensitivity analysis was conducted after regression modelling using then post-estimation statistics obtained, to verify results against unmeasured confounders (Burger and Armitage, 2006; Phillips et al., 2016). This was in-built into our regression analyses.
5. **Transparent Reporting**: transparency in reporting on methods and limitations in the study was done, to foster result reliability (Stuart et al., 2010).

In all, these steps were taken to fortify our study findings, towards ensuring robust conclusions.

3.15 Ethical Considerations

Ethical clearance was obtained from the Ensign Global College Ethics Review Committee. Confidentiality of data, privacy, and respect for individual study participants, was ensured. Data obtained was protected ethically, to ensure confidentiality and privacy of the subjects. The hard copy was kept under lock-and-key; and the electronic version of the data kept on a password protected computer accessible to only the principal investigators. Data was obtained with the consent and express permission of the management of the research site.

3.16 Limitations

Since secondary data was relied on, there was a high number of incomplete data for some of the participants of the study. Some of the demographic characteristics that would have been desired, like the educational levels, and other risks like the extent of smoking, the quantities of alcohol consumed and whether patients were alive or dead at the time of data collection could not be obtained. These limitations to some extent do limit the degree to which we can generalize our findings to the entire population. We therefore opine here that the results of our findings, even though robust, should still be applied bearing in mind these genuine limitations of the study. It also calls for prostpectively collected data in the future; to provide data that is planned to provide the exact parameter needs for such a far reaching study.

3.17 Assumptions

No assumptions were made in this study.

CHAPTER 4

RESULTS

4.1.0 Introduction

In this study, we analyzed data from 852 patients diagnosed with prostate cancer by histology (biopsy results) and attending the Sweden Ghana Medical Centre for treatment over a twelve-year period. We explored trends in patient visits, demographic characteristics, disease determinants, some indirect treatment-outcome measures, and some associations (correlations) and relationships(regression analysis) between key variables, and ended with some brief predictive modelling.

4.1.1 Determinants and Trends(Temporal, Ethnic-Rates-of-Disease) of Prostate Cancer Cases

Yearly Trends in Patient Visits: To help us understand the growing burden in prostate cancer cases we analysed for distinct trends in patient visits over the years (see Figure 4.1):

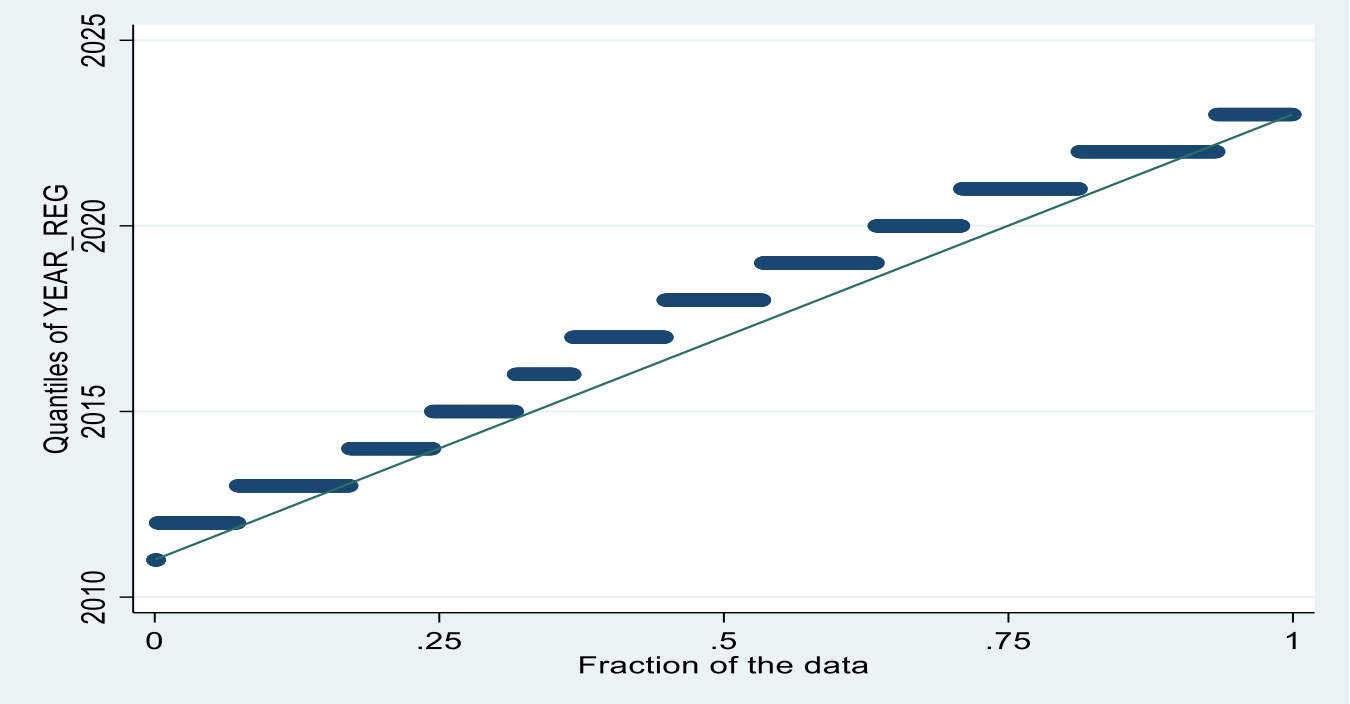


FIG 4.1: A NORMAL QUANTILE PLOT SHOWING THE SGMC, PROSTATE CANCER CASE-TRENDS, 2011 TO 2023

From 2011 to 2014, patient visits were relatively stable; 2 (0.23%) in 2011 to 62 (7.28%) in 2014. Between 2015 to 2018, patient visits continued to grow gradually, 73 (8.57%) in 2018. The final period of 2018 to 2023, saw a significant rise in patient visits, indicating an accelerating trend; with numbers exceeding 100 in 2022 (12.09%) and 103 in 2023 (6.69%). Overall, trend was a steady rise in prostate cancer cases/burden.

TABLE 4.1: Summary Statistics for Various Parametric Independent Variables

PARAMETER	Obs	Mean	Std. Dev.	Min	Max
AGE (yrs)	852	67.385	8.41	45	91
WEIGHT(Kg)	852	77.332	14.693	38.9	152.2
HEIGHT(M)	852	1.71	0.07	1.50	1.99
BMI (Kg/M^2)	852	26.571	6.396	14.53	41.42
LINEAR W-H (Kg/M)	852	44.95	7.00	24.46	72.06
PONDEREX (Kg/M^3)	852	15.46	2.62	8.54	25.18

From table 4.1, the average age of the participants was approximately 67.5 years, with a standard deviation of 8.2 years. Age ranged from a minimum of 45 years to a maximum of 91 years.

In terms of weight, the participants had an average weight of 76.8 kilograms, with a standard deviation of 12.7 kilograms. Weight ranged from a minimum of 38.9 kilograms to a maximum of 129.4 kilograms.

The participants also had an average height of approximately 1.71 meters, with a standard deviation of approximately 0.07 meters. Heights ranged from a minimum of 1.50 meters to a maximum of 1.99 meters. Body Mass Index (BMI), a key indicator of overall health, averaged at 26.3 kg/m^2, with a standard deviation of 4.1 kg/m^2. BMI values spanned from a minimum of 14.53 kg/m^2 to a maximum of 41.42 kg/m^2.

The Linear W-H ratio, which relates weight-to-height, averaged at 44.95 kg/m, with a standard deviation of 7.00 kg/m. This ratio ranged from a minimum of 24.46 kg/m to a maximum of 72.06 kg/m. Lastly, the

Ponderal Index (PONDEREX), a measure of body mass relative to height cubed, had an average value of 15.46 kg/m³, with a standard deviation of 2.62 kg/m³. PONDEREX values ranged from a minimum of 8.54 kg/m³ to a maximum of 25.18 kg/m³.

TABLE 4.2: Summary Statistics for Various Parametric Dependent Variables

PARAMETER	Obs	Mean	Std. Dev.	Min	Max
PSA AT DIAGNOSIS (ng/ml); Median value = 29.0 ng/ml	852	496.391	2240.127	.19	25000
PSA AT THE BEGINNING OF TREATMENT (ng/ml)	419	559.198	2664.561	.05	25000
DOSE OF RADIATION TREATMENT RECEIVED(Grays)	852	0.000* *(Median)	0.000* * (Mode)	0.00	78.00
LOWEST PSA / NADIR (ng/ml)	852	154.750	545.251	.020	5405.50
PSA RESOLUTION (ng/ml)	852	233.983	2065.528	-5393.28	249600
PSA PER DOSE OF RADIATION (ng/ml- per Gray)	852	31.602	905.751	-5393.28	15299.80
PSA RESOLUTION PER TREATMENT MODALITY (ng/ml)	852	228.514	2034.179	-5360.50	24960.00
HIGHEST PSA (ng/ml)	852	1210.764	3982.174	.25	25000.00
FAIL PSA (ng/ml)	128	249.514	560.037	.58	2600.00
FAIL-RESOLUTION-MULTIPLES (unitless)	852	4.579	39.794	0.00	512.80

The study analyzed various aspects of PSA levels, including PSA at diagnosis (Mean: 496.391, Std. Dev.: 2240.127), PSA at the beginning of treatment (Mean: 559.1982, Std. Dev.: 2664.561), lowest PSA (Nadir)

(Mean: 154.75, Std. Dev.: 545.251), and PSA resolution (Mean: 233.983, Std. Dev.: 2065.528). Any negative PSA resolution(or its derivative) suggests that the PSA at diagnoses failed to respond to the treatment given.

This dataset provides key information about prostate-specific antigen (PSA) levels in 852 individuals. PSA is crucial in prostate cancer monitoring.

At diagnosis, the median PSA level is 29.0 ng/ml, showing the extent of cancer. PSA levels at the start of treatment vary widely, from 0.05 to 25000 ng/ml.

As is expected, some individuals received no radiation treatment, which is why the median dose is 0.000 Grays.

The lowest PSA during treatment ranges from 0.02 to 5405.5 ng/ml, indicating different responses. PSA resolution varies widely, with an average of 233.983 ng/ml.

Examining the relationship between PSA and radiation dose, PSA per Gray ranges from -5393.28(negative values suggest an outright no-response to treatment); to 15299.883 ng/ml per Gray. PSA resolution per treatment type varies, from -5360.5 to 24960 ng/ml.

The highest measured total serum PSA values (during the disease course) range from 0.25 to 25000 ng/ml (0.58 to 2600 ng/ml).

Finally, fail-resolution multiples varied from 0 to 512.821, offering insights into treatment outcomes.

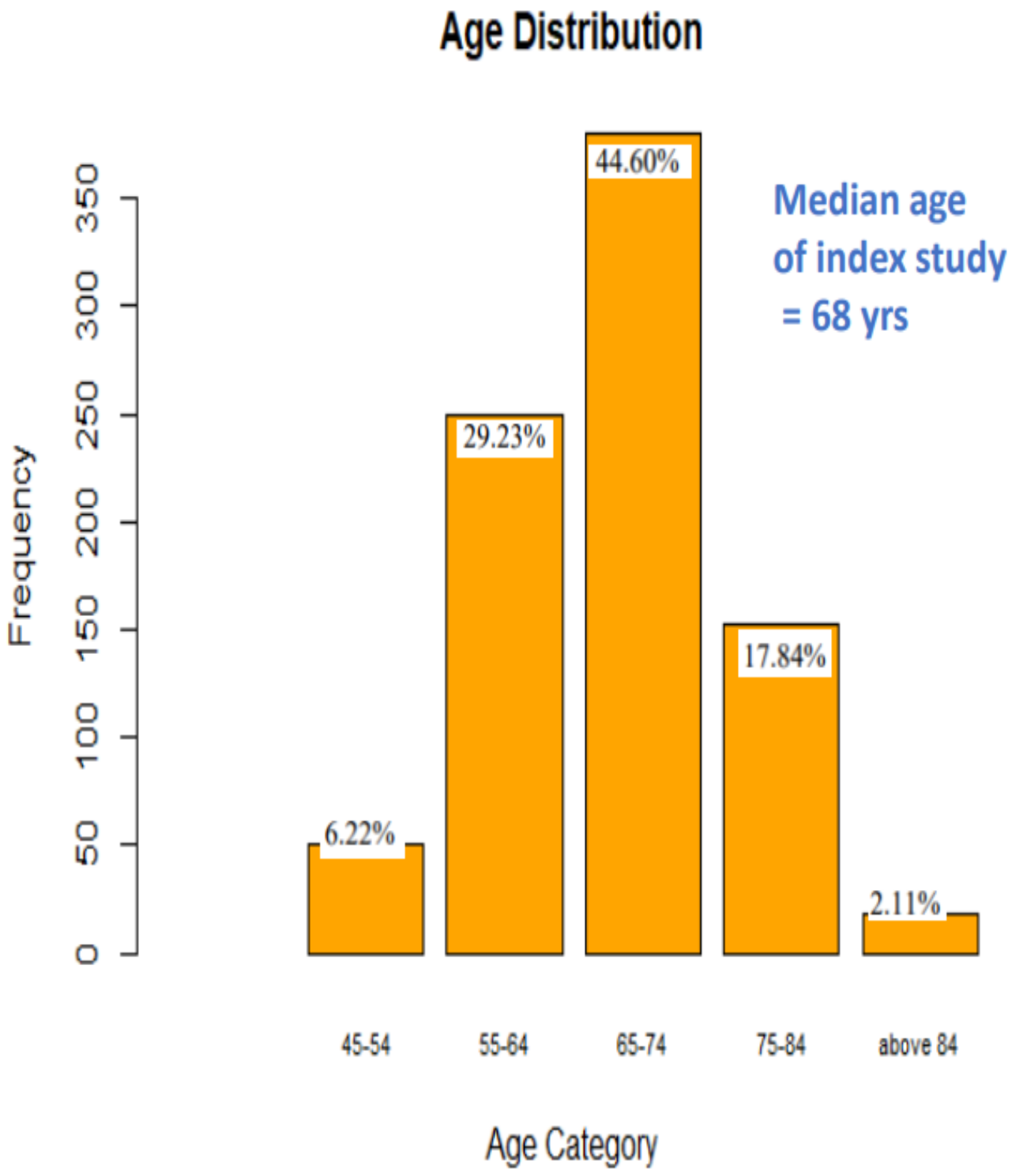
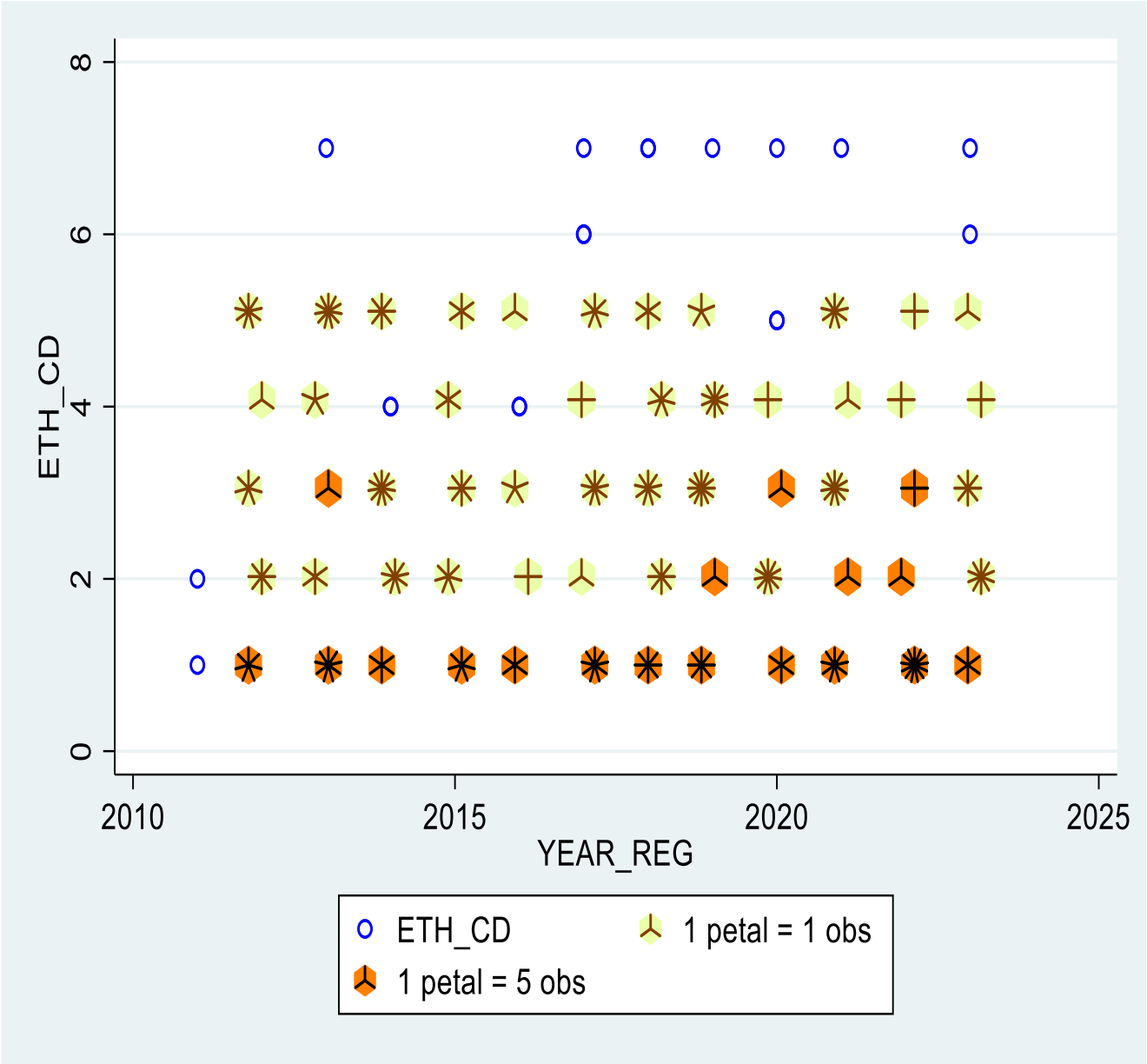


FIG 4.2 AGE DISTRIBUTION

From fig. 4.2, the ages of the clients were normally distributed. With the modal age of 65 to 74 constituting 44.69% of the population.

Ethnicity; (and Nationality): Most prostate cancer cases attending the SGMC were of people who were Akans(fig 4.4). They constituted, 55.52%. 14.91% were Ewe, 13.38% were Ga, 7.63% were northern

Ghanaians, 8.57% were Foreigners (Nigerians, Togolese, Beniniois, Burkinabes, Sierra Leoneans, Guineans, Ivorians, Jamaicans, Caucasians, Asians).



ETHNICITY (1)AKAN, (2)EWE, (3) GA, (4)NORTHERN GHANAIAN MEN, (5)NIGERIANS (6)OTHER AFRICANS/JAMAICANS (7) CAUCASSIANS/ASIANS.

FIG 4.3 A DENSITY – DISTRIBUTION SUNFLOWER PLOTS FOR TIME-TRENDS AMONGST ETHNIC GROUPS OVER THE STUDY PERIOD;

NB: THE DARKER THE PETAL AND THE MORE THE SPOKES/ RADIATES, THE LARGER THE NUMBER OF OBSERVATIONS IN IT.

This density- distributional sunflower (trend) diagram, (FIG 4.3) above shows a gradual increase in cases over the years amongst the various ethnic groups, but still depicts the observation that Akans predominated throughout the period under study.

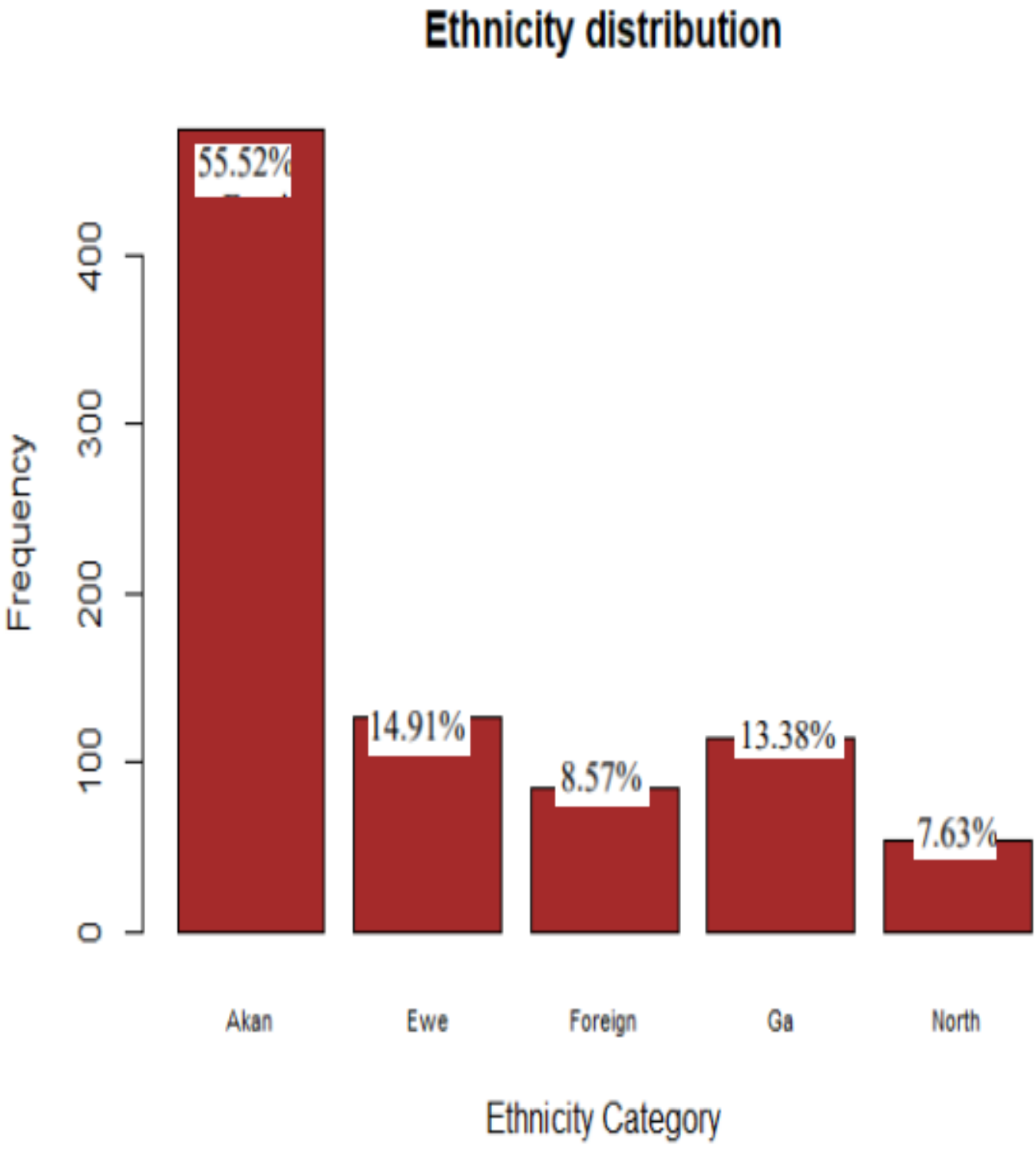


FIG 4.4 DISTRIBUTION OF THE ETHNICITY OF STUDY GROUP

The question we asked ourselves in this study after obtaining these percentages (for the ethnicity case-

proportions) was whether these ethnicity percenages were different from the general proportions of distribution of the ethnicities in Ghana; and whether there were any statistically significant differences; or any observed differences were by chance. So we set out to conduct simple two-proportion z-test between the observed SGMC prostate cancer case-proportions and the Ghanaian population's distribution for the ethnicities according to the 2021 Ghana Population and Housing Census. The summary is presented below; and the details of the calculations are presented at the Appendix 4 of the main thesis.

Given that:

1. **Sample Size at SGMC POPULATION OF GHANAIAN MEN (ONLY) WITH PROSTATE CANCER FROM SGMC):** 776. This is from the index study.
2. **Sample Size in Ghana(POPULATION OF MEN AGED >/=45 IN GHANA):** 3,377,818 (GPHC, 2021).

TABLE 4.3a: Test of Difference between two Proportions (Ethnicity case-proportion at SGMC, versus each National Ethnicity's proportion, separately)

Ethnic Group	Proportion at SGMC (%)	Proportion in Ghana (%; [**GPHC]) 2021)**	Test Statistic (Z)	P-value
Akan	55.52	47.5	12.897	<0.05
Ewe	14.91	13.9	-0.775	>0.05
Ga	13.38	7.4	8.721	<0.05
Northern Ghanaian	7.63	29.5	-34.652	<0.05

Conclusion: Based on the corrected sample size of 776 for Ghanaian men attending SGMC Hospital with prostate cancer, there is strong statistical evidence to suggest a significant difference in the proportions of Akan, Ga, and Northern Ghanaian men compared to the respective population proportions in Ghana. However, for Ewe men, there isn't enough statistical evidence to conclude a significant difference(table 4.3).

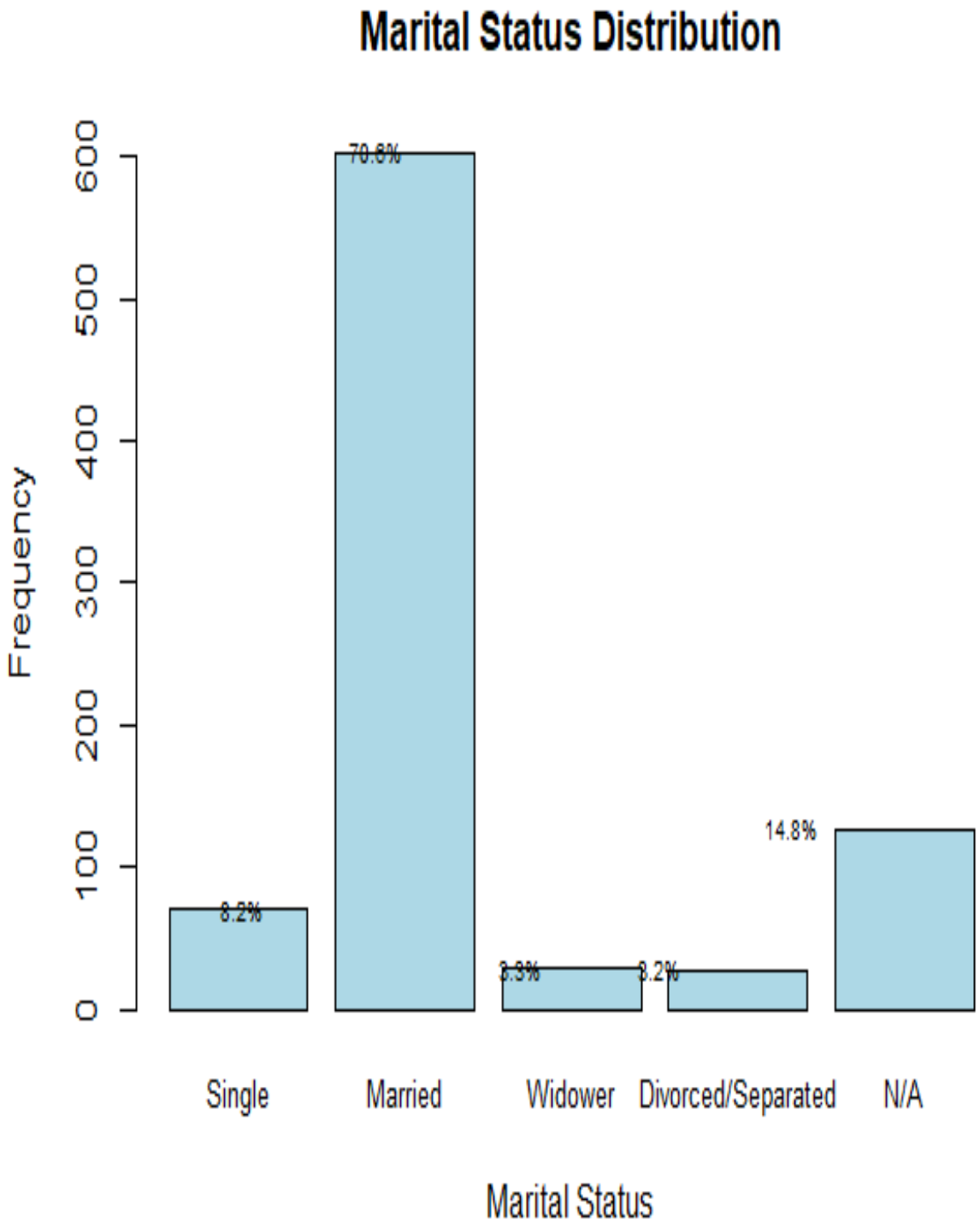
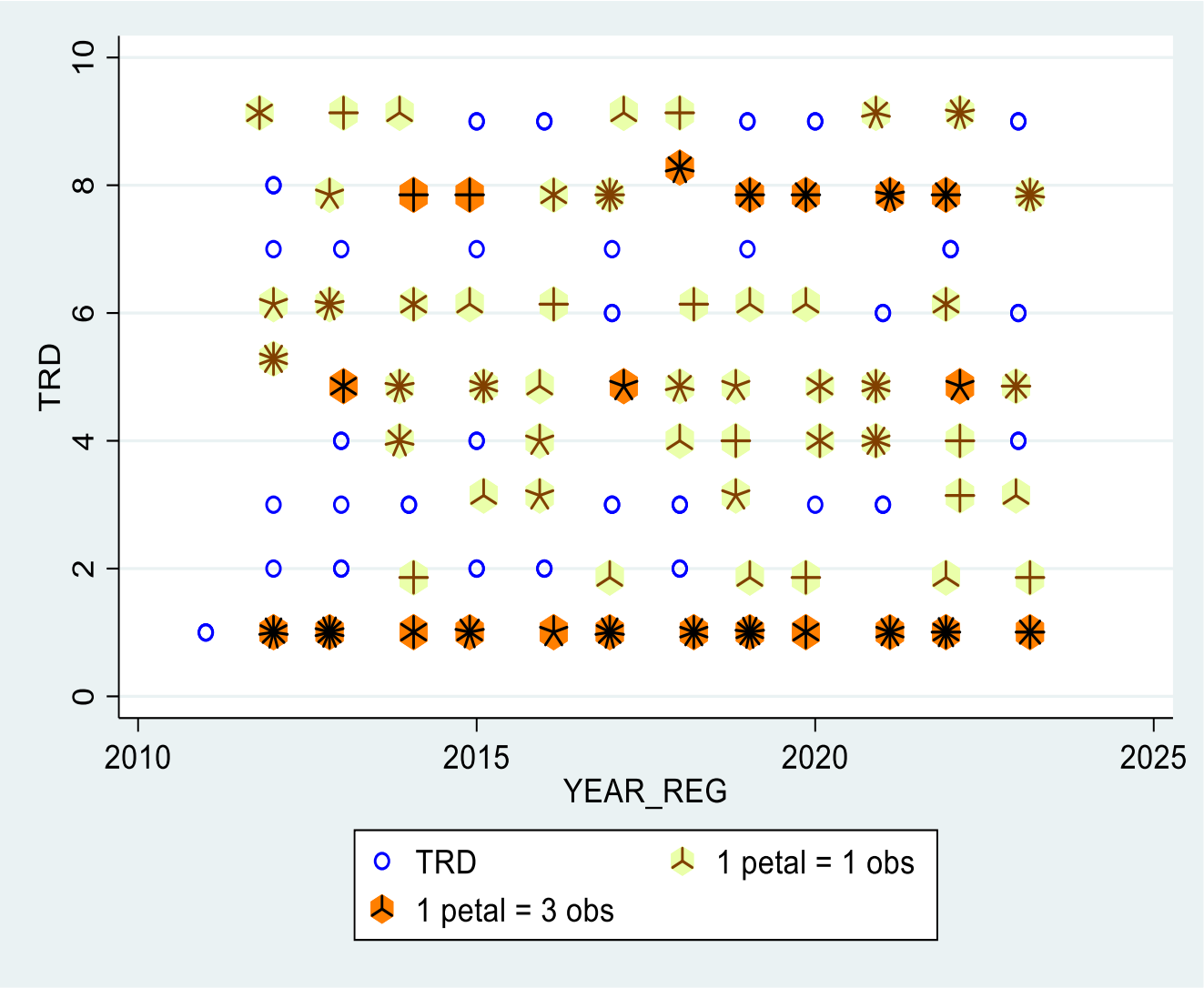


FIG 4.5 MARITAL STATUS DISTRIBUTION

Most of the clients were married; 70.6% (table 4.3a , and fig 4.5 under appendix 4).

Most of the study participants had a high socio-economic status**,** (59.40%), followed by (13.50%) with a low socio-economic status (table 4.3a, and fig 4.6 at appendix 4). The rest were "Retired/data not

available", together, (27.10%).



KEY_TRD: (1)ACADEMICS, (2)BUSINESSMEN, (3)CLERGY, (4)FORCES, (5)MANUAL, (6)PROFESSIONALS.

FIG 4.9: A DENSITY- DISTRIBUTIONAL SUNFLOWER PLOT SHOWING TIME-TRENDS FOR PROSTATE CANCER AMONGST THE VARIOUS OCCUPATIONAL GROUPS.

NB: THE DARKER THE PETAL AND THE MORE THE SPOKES/ RADIATES, THE LARGER THE NUMBER OF OBSERVATIONS IN IT.

This density- distributional sunflower (trend) diagram (fig 4.9) depicts that, amongst the occupations, the

cases were predominant amongst the professionals' occupational group, a general trend that persisted over the study period.

TABLE 4.3B SUMMARY TABLE FOR CATEGORICAL VARIABLES FOR DISEASE DETERMINANTS.

ATTRIBUTE/ PARAMETER; and VARIABLES								TOTALS
OCCUPATION AS TRADITIONALLY CLASSIFIED								
ACADEMICS	BUSINESS -MEN	CLERGY	FORCES	MANUAL	PROFESSIONALS	RETIRED /NOT STATED	UNEMPLOYED	TOTAL
3.52%	5.74%	3.63%	5.28 %	13.60%	40.33%	27.06%	0.84%	100 %
SOCIO-ECONOMIC STATUS (SES) BASED ON OCCUPATIONS*								
LOW SES	HIGH SES	RETIRED	NOT STATED				TOTAL	
13.5%	59.4%	21.7%	5.4%				100%	
ACTIVITY LEVELS BASED ON OCCUPATIONAL*								
SEDENTARY	NON-SEDENTARY	-	RETIRED /NOT STATED/NA				TOTAL	
31.07%	43.85%	-	24.08%				100%	
BMI CATEGORIES								
UNDERWEIGHT	NORMAL BMI	OVERWEIGHT	OBESE/ MORBIDLY OBESE				TOTAL	
4.23%	26.9%	53.4%	16.08%				100%	
SMOKING HABIT								
	YES		NO	NOT STATED			**TOTAL**	
	8.6%		81.8%	9.6%			100%	
ALCOHOL HABIT								
	YES		NO	NOT STATED			TOTAL	
	31.3%		61.2%	7.5%			100%	

***See A`ppendix 4 for the general guidelines for assigning these criteria from occupations.**

Based on activity levels related to occupation, 31.07% were sedentary, 43.85% were non-sedentary; and 24.09% were retired or had data on that not available (table 4.3b).

Most of the clients, 40.33% were professionals, 13.60% engaged in manual work, 5.74% were businessmen, and 5.28% serve in forces such as the military or police. Additionally, 3.52% were academics, 3.63% were clergy members, and a significant portion, 27.06%, were either retired or did not have their occupations specified in the data available. A small percentage, 0.82%, were unemployed (table 4.3b).

From table 4.3a, above, a majority of the men in the study were overweight 53.4%. Out of the remaining, 26.9% were of normal weight, 4.23% were underweight and the remaining 16.08% were obese or morbidly obese. 81.8% of the study participants were non-smokers. Smokers constituted 8.6%; and the rest did not have data available (table 4.3b). From the same table, we realise that apart from the 7.5% of the study participants that did not have data on alcohol intake available, 31.3% did drink some alcohol. 61.2% did not drink any alcohol (also see fig 4.12 under appendix 4). The percentage of smokers was much smaller, at 8.6%, (table 4.3b); with the rest either not smoking or not having records on that.

TABLE 4.4 Distribution of Comorbidities amongst the Patients

COMORBIDITY	FREQUENCY	PERCENTAGE	CUMMULATIVE PERCENTAGE
None	669	78.43	78.43
Hypercholesterolaemia Alone	1	0.12	78.55
Diabetes Alone	17	1.99	80.54
Hypertension Alone	90	10.55	91.09
Hypertension And Hypercholesterolaemia	2	0.23	91.32
Hypertension And Diabetes	35	4.10	95.43
Hypertension, Diabetes, Hyperholesterolaemia	2	0.23	95.66

Haematuria/UTI	7	0.82	96.48
Various Others (Asthma, Msp, ED, Obesity, Weakness, PUD, Gout….)	30	3.52	100.00
Total	**853**	**100.00**	

Amongst our study participants, 78.43% did not have any comorbidities at all. Of those that had co-morbidities, hypertension predominated, with a combined percentage of 15.11% in various combinations with its other allied co-morbiditie: diabetes, hyperlipidaema/hypercholesterolaemia, obesity and heart disease. Unexpected conditions like anaemia due to haematuria with urinary tract infections featured as well in 3.52% (table 4.4).

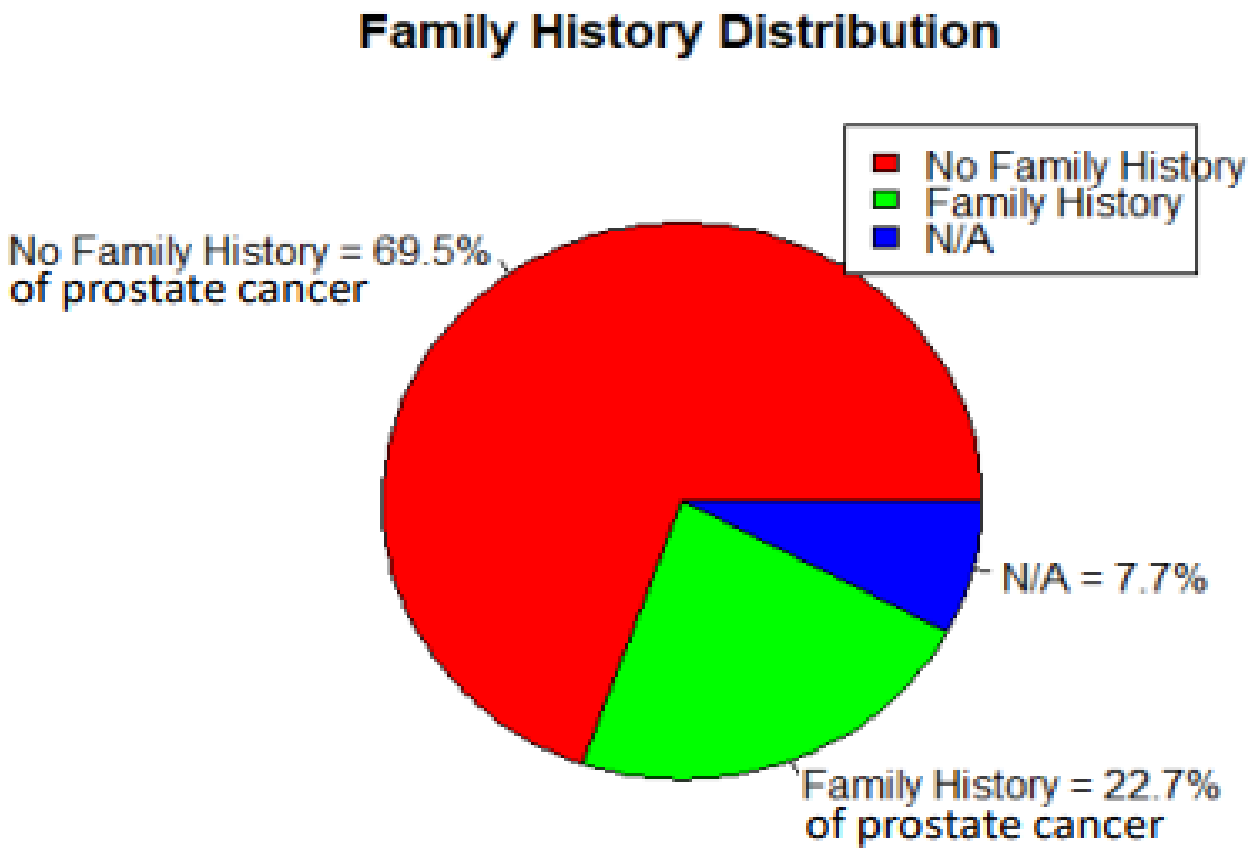


FIG 4:13 FAMILY HISTORY OF PROSTATE CANCER AMONG STUDY GROUP

22.7% of study participants had records indicating the presence of prostate cancer in a male relative. 69.5% did not have any such history; and 7.7% did not have data available (fig 4.13).

4.2a Determinants of Prostate Cancer Disease Severity Inherent to the Disease at Diagnosis

Concerning inherent risks (for localised disease) that depict disease severity and likelihood of treatment success based on PSA at diagnosis, 50.42% had low risk disease, and 33.05% had high risk disease. 16.53% had an intermediate risk disease. Digital Rectal Examination (DRE) categorization of the same property yielded similar results: low risk, 53.19%l; high risk, 29.42%, and intermediate risk, 17.38% (fig 4.14).

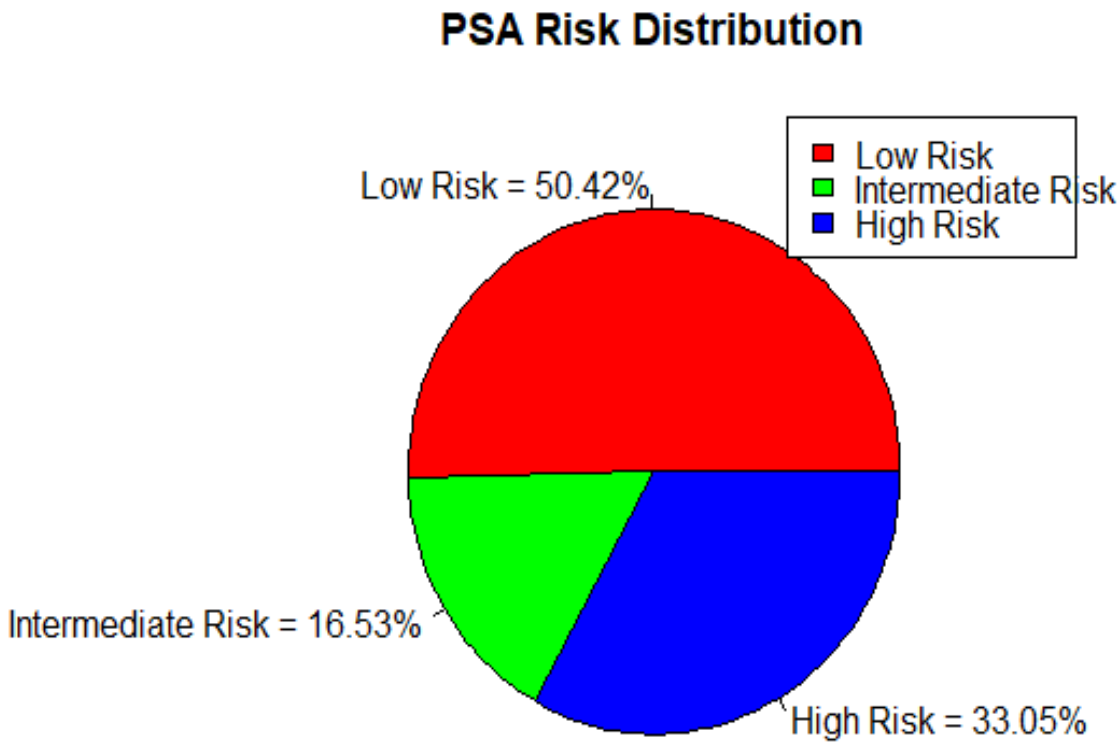


FIG 4.14 PSA RISK STRATIFICATION OF DISEASE

TABLE 4.3C: SUMMARY TABLE FOR DISEASE SEVERITY, TREATMENT MODALITIES AND TREATMENT OUTCOMES

DISEASE RISK STRATIFICATION BY PSA			
LOW RISK	INTERMEDIATE RISK	HIGH RISK	TOTAL
50.42%	16.53%	33.05%	100%

DISEASE RISK STRATIFICATION BY DRE			
LOW RISK	INTERMEDIATE RISK	HIGH RISK	TOTAL

53.19%	17.38%	29.43%			100%	

ISUP GRADES DISTRIBUTION					
GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5	TOTAL
19.13%	21.48%	19.50%	20.58%	19.31%	100%

DISEASE RISK STRATIFICATION BY HISTOLOGY (GLEASON SCORE/ISUP)			
LOW RISK	INTERMEDIATE RISK	HIGH RISK	TOTAL
46.67%	36.03%	17.06%	100%

DISEASE TREATMENT; MODALITIES							
TYPE OF ADJUVANT/ALLIED THERAPY GIVEN TO THE PATIENTS							
NONE	BRACHY THERAPY	CHEMO THERAPY	CHEMO-RADIATION	CHEMO and SURGERY	GOLD SEEDS	SURGERY MAIN; AND ALLIED	TOTAL
65.12%	3.72%	8.85%	0.18%	3.54%	4.07%	14.52%	100%

TOTAL NUMBER OF ADJUVANT THERAPY GIVEN PER PATIENT			
None	One	Two	TOTAL
65.12%	16.59%	18.29%	100%

DISEASE TREATMENT OUTCOMES			
HIGHEST PSA PEAK DURING TREATMENT PERIOD; CATEGORISED (ng/ml)			
10 or less	10 to>100		TOTAL
8.33%	91.67%		100%

PSA RESOLUTION PER NUMBER TOTAL OF TREATMENT MODALITIES GIVEN (ng/ml-per modality given)			
<0.5	0.5 to 20	>20	TOTAL
41.78%	26.76%	31.96%	100%

LOWEST PSA ATTAINED DURING TREATMENT PERIOD (NADIR); CATEGORISED (ng/ml)			
<0.5	0.5 TO 4	>4	TOTAL
22.30%	31.81%	45.89%	100%

FAIL-PSA-REFRACTORY MULTIPLES (FAIL PSA DIVIDED BY LOWEST PSA) (ng/ml)					
<3	3.5 to 10	10.5 to 20	20.5 to 100	>100	TOTAL

49.2%	28.8%	0.1%	18.0%	3.9%	100%

In our prostate cancer study group (table 4.3c; and fig. 4.15 at appendix 4), the International Society of Urological Pathology (ISUP) grades were observed as follows: out of the total of 554 that had data on this attribute available, Grade 1 was represented by 106 cases, constituting 19.13% of the total; Grade 2 had 119 cases, accounting for 21.48%; Grade 3 was comprised of 108 cases, making up 19.50% of the total. Grades 4 and 5 were represented by 114 cases (20.58%) and 107 cases (19.31%), respectively (table 4.3c; and fig 4.16 under appendix 4).

Localised prostate cancer disease risk/severity categorization by histology on prostate core biopsy, yielded the following risk strata for our 852 study participants; 46.37%: low risk; 17.6%: high risk, 36.03% intermediate risk (see table 4.3c above, and fig 4.17 at appendix 4).

Putting all the three risk categorization parameters, PSA, DRE and ISUP together, for comprehensiveness and completeness of disease severity classification in localised prostate cancer, we arrived at an overall risk categorization distributions of low risk, 29.56%, intermdiate risk, 25.69% and high risk, 44.75% (fig 4.18). Among the 852 cases, 71.38% showed no evidence of metastasis while 28.72% had metastatic diseease. Subgroup analysis of the non-metastatic prostate cancer disease, showed that 53.19% had localised disease and 17.39% had locally-advanced disease. Late stage disease rate was therefore, 46.81%. Amongst the localised non-metastatic disease, we had the following overall disease risk/severity assessment outcomes: 44.75% were "High risk," 25.69% were "Intermediate risk," and 29.56% were "Low risk" diseases (fig 4.19).

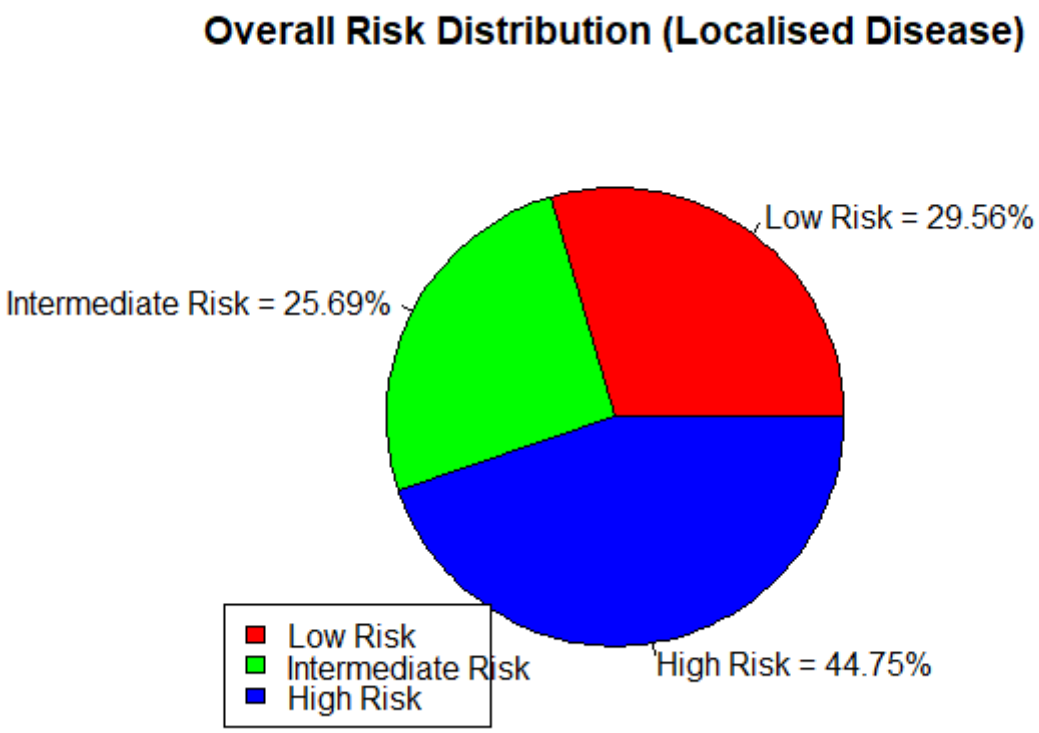


FIG 4.18 OVERALL PROSTATE CANCER RISK CATEGORIZATION

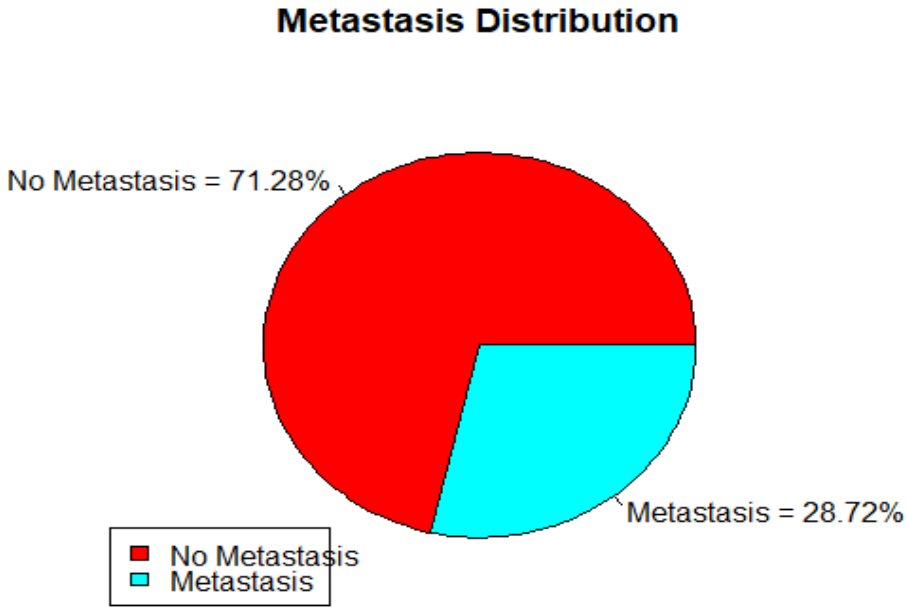


FIG 4.19 DISTRIBUTION OF METASTATIC PROSTATE CANCER IN THE STUDY GROUP

The metastatic prostate cancer disease rate was 28.72% over the period of study (fig 4.19).

KEY MET_CD: 0= NO METASTASIS; 1 = METASTASIS

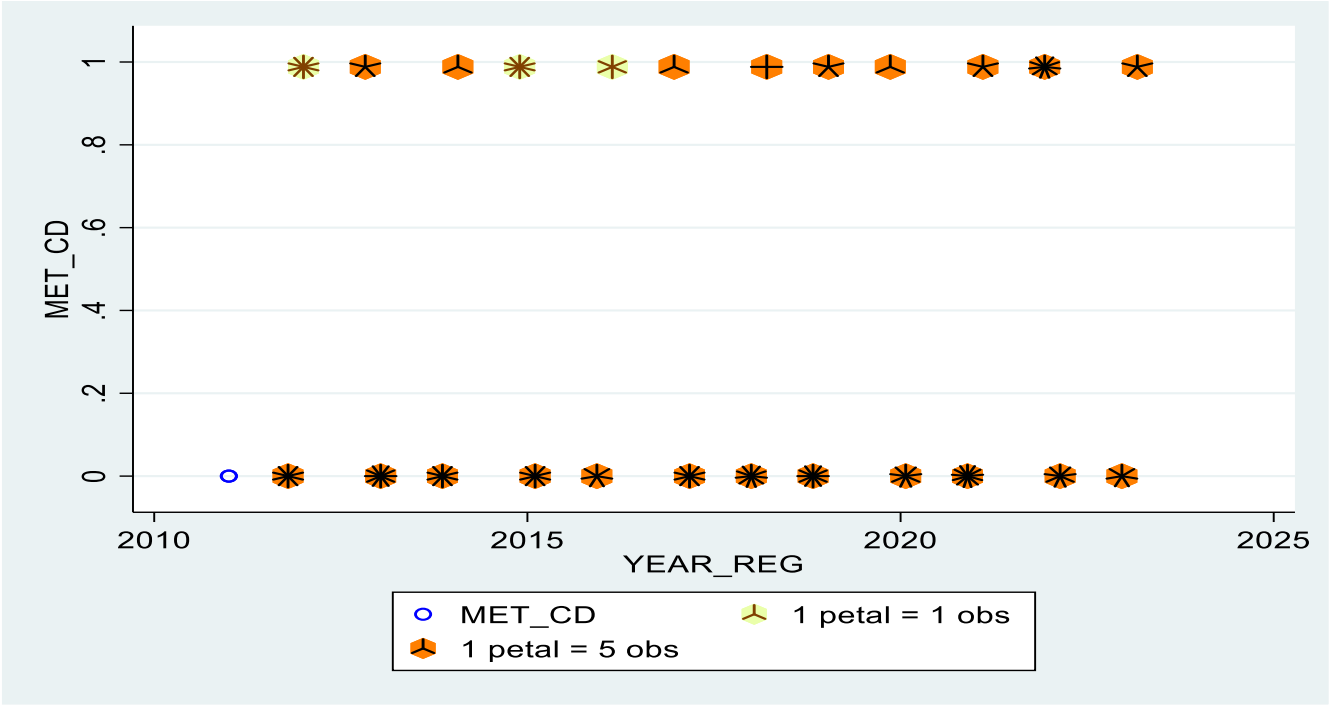


FIG 4.20: DENSITY- DISTRIBUTIONAL SUNFLOWER PLOT SHOWING TIME-TRENDS FOR METASTASISED AND NON-METASTASISED PROSTATE CANCER CASES OVER THE STUDY PERIOD

NB: THE DARKER THE PETAL AND THE MORE THE SPOKES/ RADIATES, THE LARGER THE NUMBER OF OBSERVATIONS IN IT.

This density- distributional sunflower (trend) diagram,(fig 4.20) suggests that over the years, as the total number of prostate cancer patients increased, the number or proportion of metastatic prostate cancer patients also increased in unison.

The types of adjuvant therapy, that clients benefited from at the SGMC over the study period were bracchytherapy (3.72%), chemotherapy (8.85%), gold-seed insertion to guide radiation therapy (4.07%), and surgery (14.34%); and allied-surgery of various kinds (0.18%). Another 0.18% had chemoradiation, 3.54% had chemotherapy and surgery (see table 4.3c above, and fig4.21 under appendix 4).

We found out that 79.48% of the patients did not need any adjuvant treatment. Of the remaining that took some adjuvant treatment in addition to their primary treatment, 18.29% had only one additional modality;

whilst the last 2.23% had a combination of two adjuvant modalities see table 4.3c (and fig 4.22 under appendix 4).

Very high PSAs during treatment often suggests that there may be a big challenge with disease eradication; and in our study group, concerning the highest PSAs 8.33% had a highest PSA value of up to less than 10 ng/ml. These may be said to represent the good group (absolutely low risk in terms of PSA). The rest, 91.97% did have their highest PSAs ranging from more than 10 to >100 ng/ml (and even some had values of up to 25000 ng/ml; 1.88% from the raw data [please see table 4.3c above, and fig 4.23under appendix]).

Apart from its myriad other uses, PSA provides a measurable parameter for follow-up of patients; and gauging how well a prostate cancer patient is responding to a certain modality of treatment for the disease.

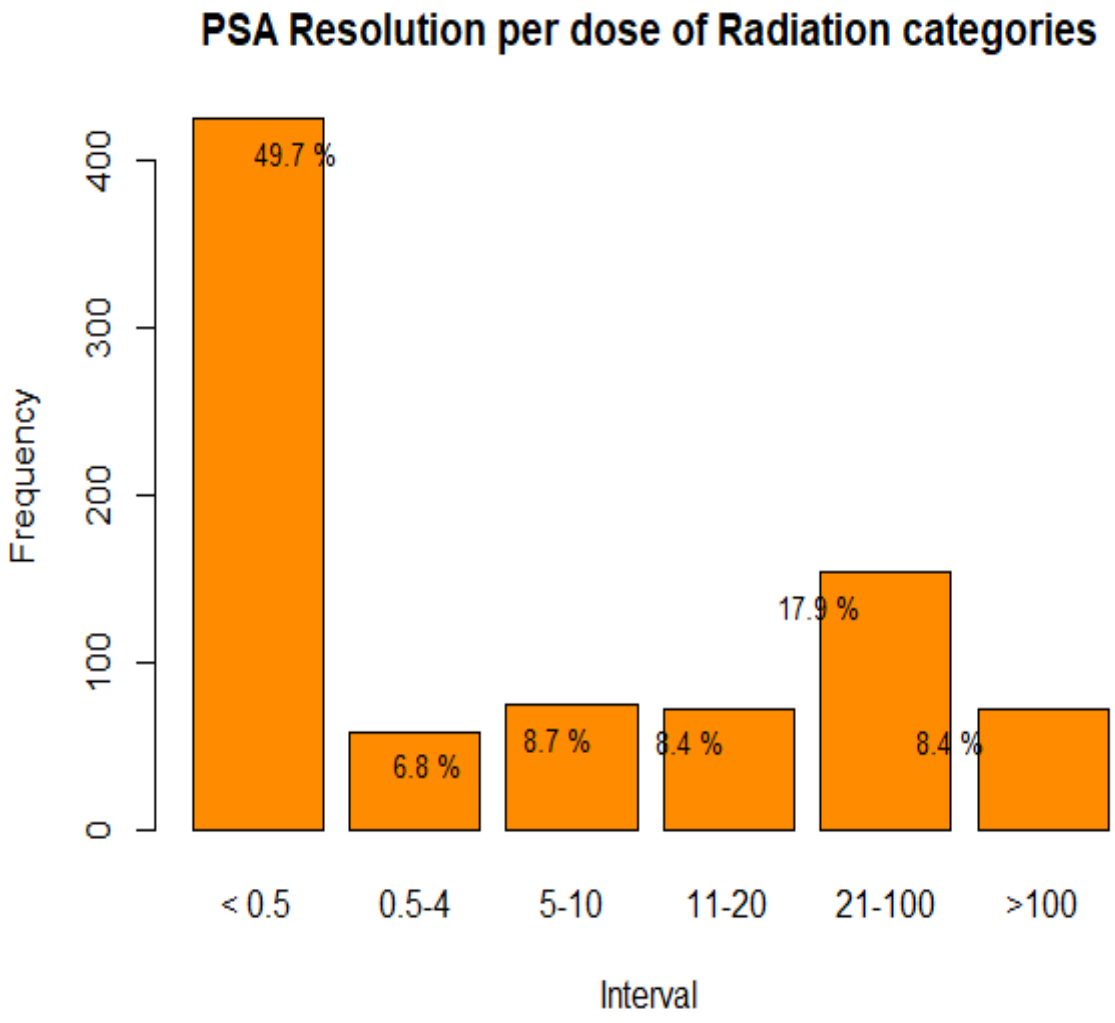


FIG 4.24 TREATMENT OUTCOME: PSA RESOLUTION PER DOSE OF RADIATION GIVEN

For determining per-input treatment respone, we calculated PSA Resolution per Grays of radiation given for those that received radiotherapy, and found out that most of them, 49.7% experienced a reduction of less than 0.5ng/ml/Gray of radiation given; representing some form of failure. The moderate responders (6.8% of the study group) had some response of 0.5 to 4 ng/ml/Gray of radiation given. The best responders (43.8%), had responses from 4 to greater 100ng/ml fall in PSA per Gray of radiation treatment given (fig 4.24).

Concerning the level of PSA Resolution per number of treatment modalities given, 41.78% had values less than 0.5ng/ml per modality (representing a failure of response to treatment of some sort). 26.76% showed some good response of 0.5 to 20 ng/mls fall in PSA per modality. The best responders who had a response of more than 20ng/ml-fall in PSA per-modality given constituted 31.97% (table 4.3c; and fig 4.25 under appendix 4).

The lowest PSA attained by a patient during the course of treatment for prostate cancer is very vital to clinicians who treat prostate cancer. It provides us with a marker for success of treatment, and also a baseline value, to promptly pick-up any looming treatment failures. A lowest PSA of 0.5ng/ml and below (and 0.2 ng/ml) by some authorities (NCCN Guidelines, 2020) is/are often used as the reproducible baseline, and any rises above that are considered worrisome and monitored or addressed. In addition, any rise in PSA greater than three-times the Nadir provides a redline indicator of failure (NCCN Guidelines, 2020).

From our study (table 4.3c, and fig 4.26 under appendix 4), 22.30% had a lowest PSA (LPSA) value (also called the Nadir) of less than 0.5ng/ml, 31.81% had a Nadir value of 0.5ng/ml to 4ng/ml; and the rest, 45.89% had a Nadir value of greater than 4 ng/ml. This means outrightly, that only 22.30% did well on treatment, based on a rise from baseline nadir to a value greater than 0.5ng/ml alone. Combining the apparent failure rates from here ie 77.7% with the failure rate based on those that had their Nadir rising by more than three times its original value (see fig 4.26); [FRM >3] will give us the overall failure rate. (FRM means Failed-Refractory Multiples; ie failed PSA divided by LPSA or the Nadir). When we combine these two probabilities (with Bayes' Theorem, and using the stata command: gen combined_condition = (FRM > 3) | (LPSA > 0.5) tab combined_condition), we arrive at an initial treatment failure rate of 77.1% (table

4.5) for this special study group, using the stated criteria preceeding. The explanation for the combination and table is below.

TABLE 4.5: Table of Output for Stata Command:

gen combined_condition = (FRM > 3) | (LPSA > 0.5) tab combined_condition

Combined_condition	FREQUENCY	PERCENT	CUMULATIVE
0	195	**22.89**	22.89
1	657	77.11	100.0
TOTAL	**852**	**100.00**	**100.00**

In our dataset, we examined a combined condition based on two variables, 'FRM' and 'LPSA.' The table displays the frequency distribution of this combined condition. A value of '0' indicates that the combined condition is not met; while a value of '1' indicates that the condition is met. Among the cases analyzed, 22.89% did not meet the combined condition (value '0'), while the remaining 77.11% satisfied the condition (value '1'). In total, 852 cases were included in the analysis. However we do not judge treatment failure based on laboratory tests alone; but also on the clinical outlook of the patient and radiological outcomes; so important though the above may be, it should be interpreted carefully. Apart from this, it may only mean that the majority of our patients present for the first time to the hospital, very late in their disease stage, as already suggested from figures 4.15 and 4.19 that, that up to 46.81% of all cases report late. With about two-thirds of this value already reporting with metastatic disease.

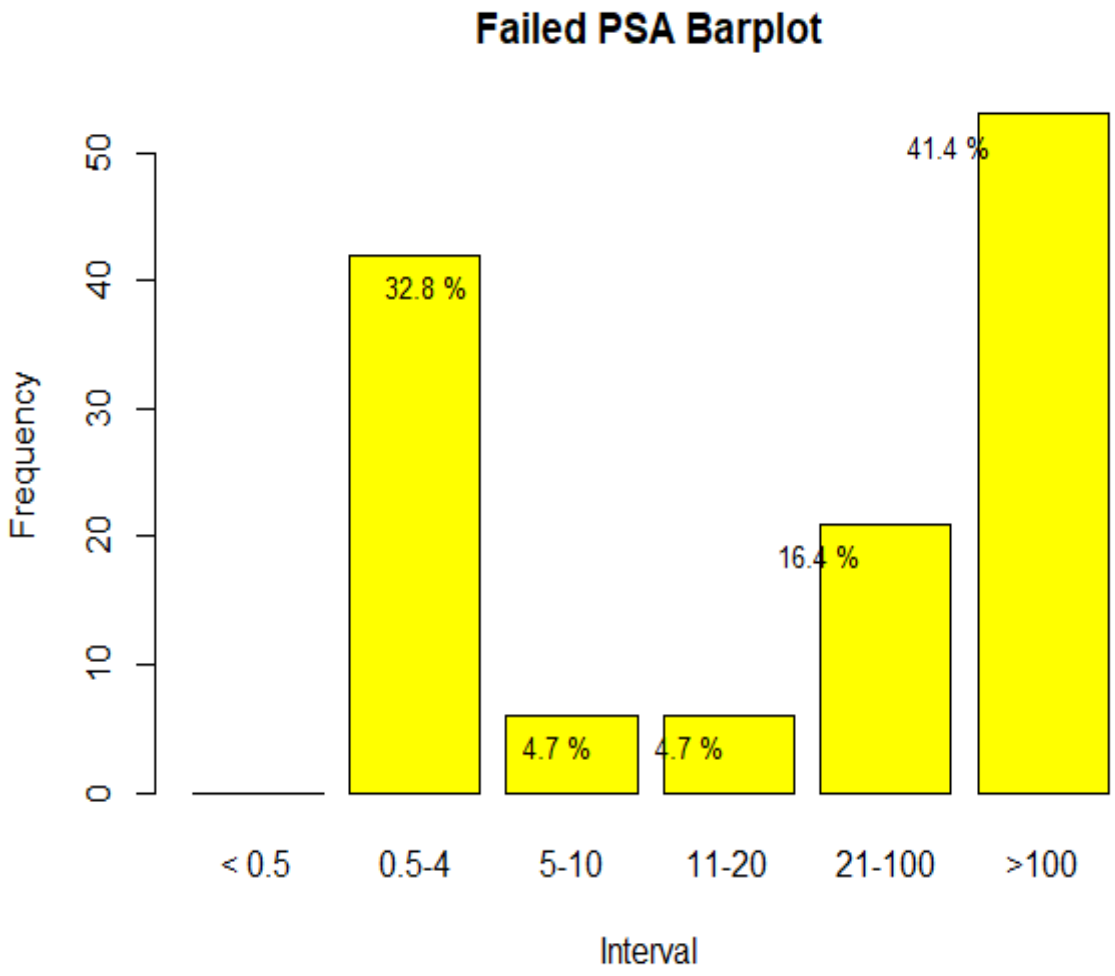


FIG 4.27 BAR CHART FOR FAIL PSA VALUES

For the group that overtly failed treatment, a majority, 57.8% were observed to have a fail PSA value of more than 20 ng/ml. When we calculated the fail PSA as multiples of the Nadir, we found out that 49.2% were still salvagable, having the failing PSAs, still within less than 3 times the Nadir (the lowest ever attained PSA during the treatment period). The remaining 50.8% did fail overtly based on this indirect measure of treatment outcome (fig 4.27).

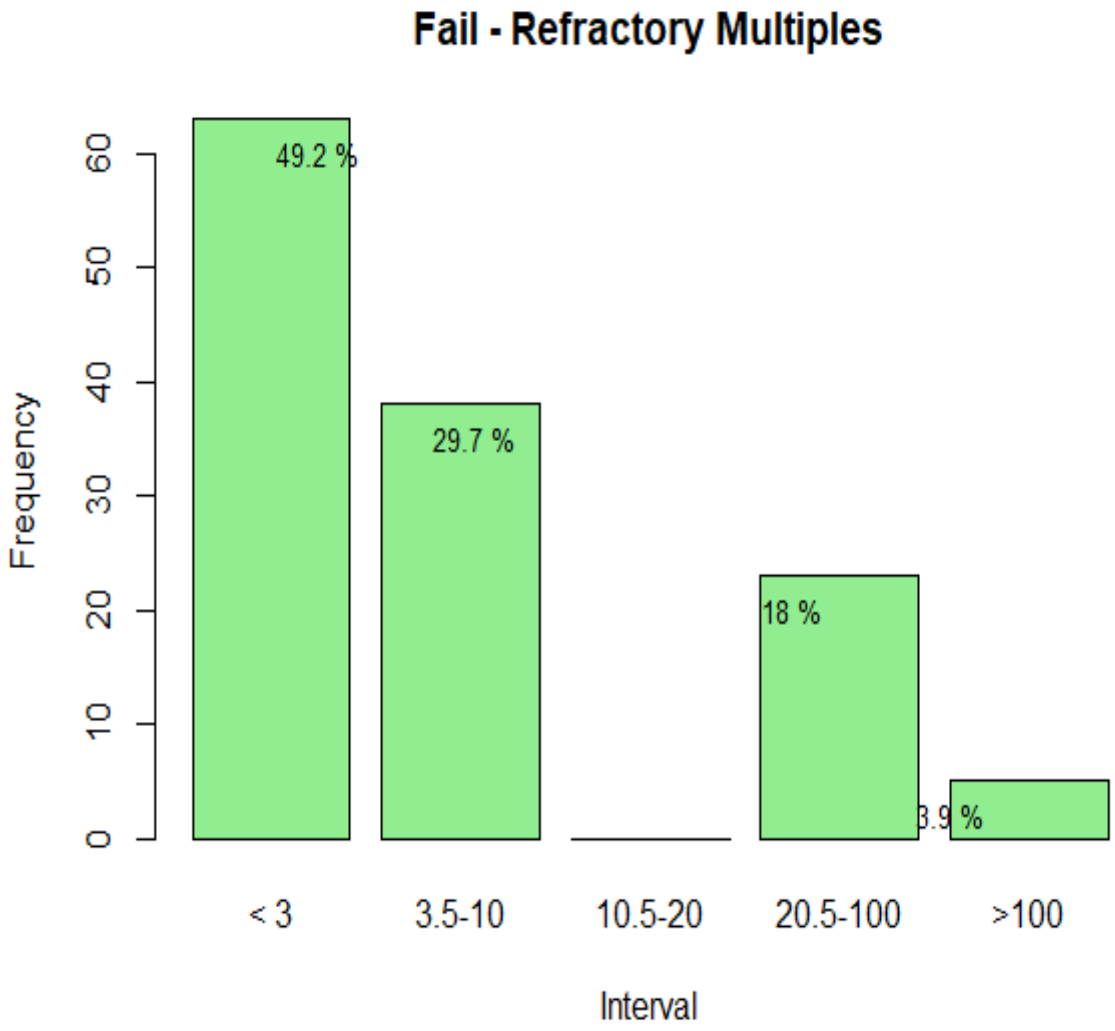


FIG 4.28A TREATMENT OUTCOME MEASURE; FAIL-REFRACTORY MULTIPLES

On assessing the proportion of the patients that had some response to therapy based on PSA, we invoke the definition that classifies a fifty percent or more, fall of the PSA from the baseline, represents a response to treatment. Based on this, we find that, 46.19% (387 out of 852) FAILED TO RESPOND; ie failed to attain at least a 50% drop in PSA at diagnosis; from the baseline; whilst 53.81% (465 out of 852) did respond, based on the definition (see fig 4. 28b, below). These values are similar to the late disease rate of 47.66% in this study, versus the early disease rate of 52.34%.

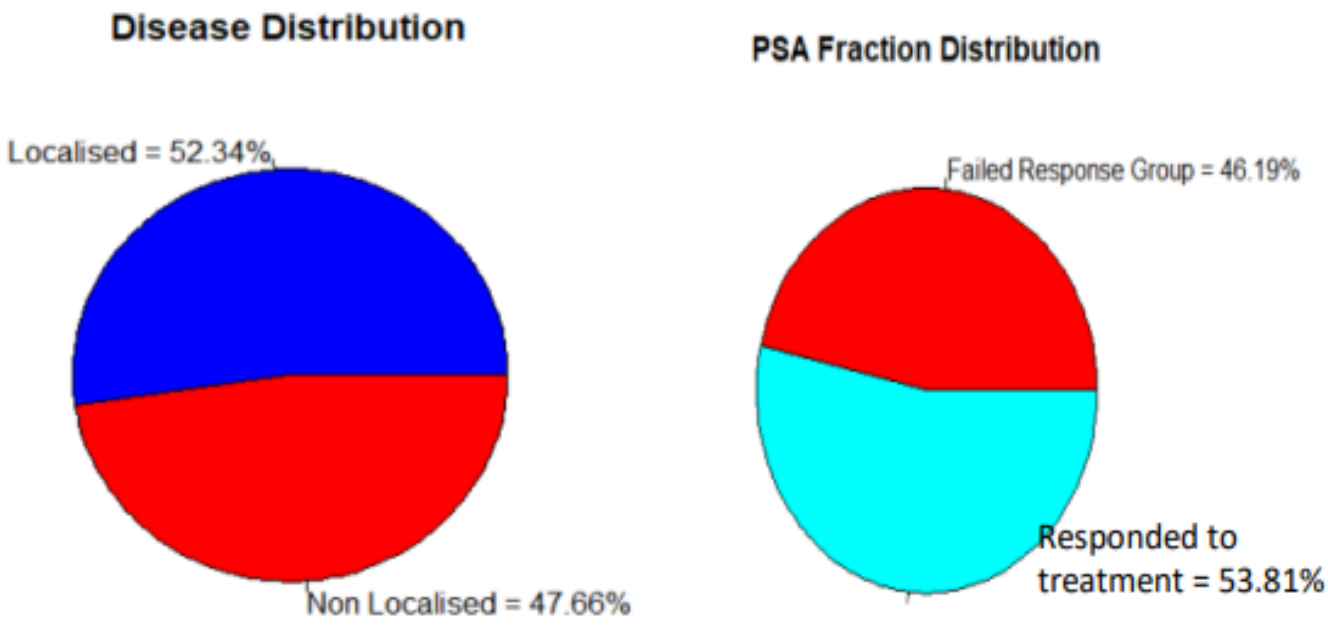


FIG 4.28A: TREATMENT OUTCOME; RESPONSE RATE, BASED ON AT LEAST A 50% PSA RESPONSE ON TREATMENT, JUXTAPOSED WITH DISEASE STAGES AT PRESENTATION; LOCALISED OR NON-LOCALISED/ADVANCED.

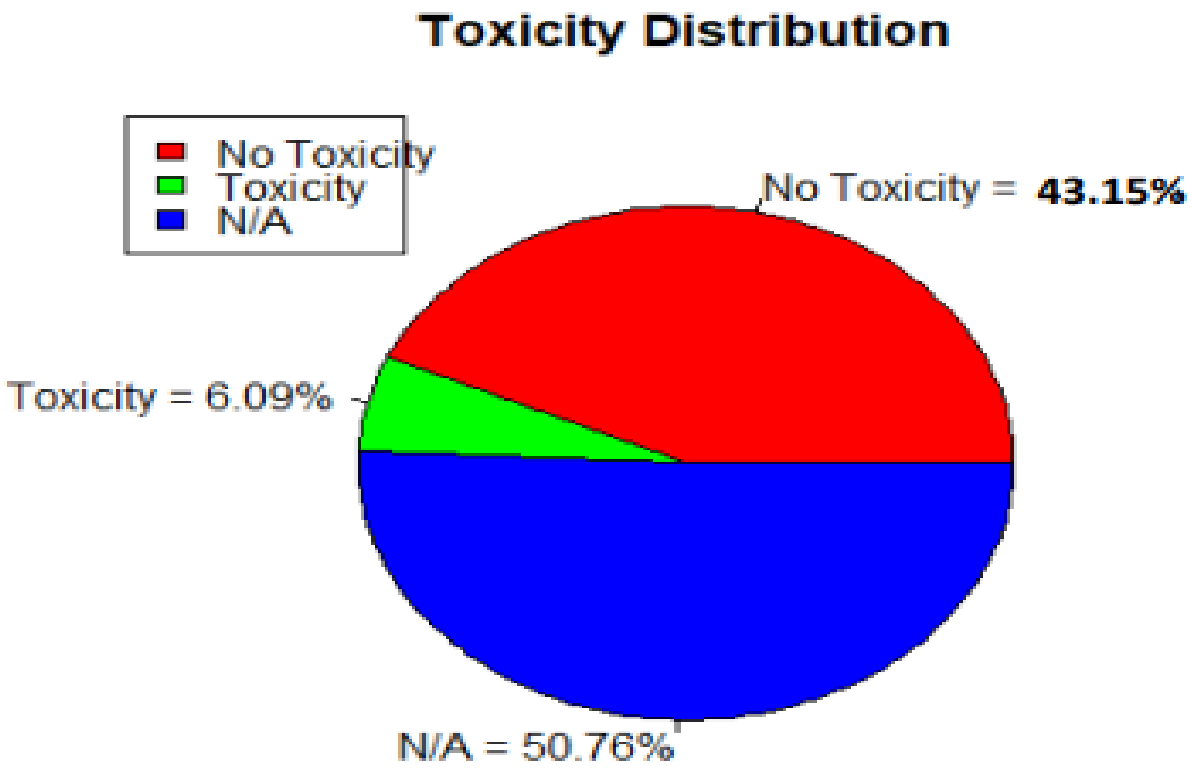


FIG 4.29 TREATMENT OUTCOME: PIE CHART FOR TOXICITY INCIDENCES

Out of the patients studied that had data on treatment toxicities available, only 6.09% had developed some toxicity. 43.15% had no toxicity incidences recorded. The majority, 50.76% had toxicity data not available fig 4.29).

4.2b Summary of Determinants of Prostate Cancer Disease:

From the descriptive statitistics, it appears that the various determinants of prostate cancer include; sex; maleness, 100%(all our patients in the study group, were males); age 55 and above (75%); modal age, 65 to 74(44.6%); ethnicity; (Akan; 55.52%, Ewe, 14.91%); high PSA, BMI above 24.5Kg/m^2 (79.48%); but overweight alone is (59.3%): married men; (70%); high socio-economic status,(59.3%); 'professional' occupation group; (40.38%; but also retirees, 21.60%). Urban residence; which was prevalent among patients (74.79%), and (PSA) a median PSA of 29ng/ml and above; which explained more than fifty percent of all the cases; and a PSA of 12.9 ng/ml and above, which explained 75% of the cases ie (the 75^{th}. Percentile).

4.2c Tests of Relationships Between Prostate Cancer and its Determinants:

The logistic regression analysis that follows this section elucidates the factors influencing prostate cancer risk. Each variable's odds ratio and associated p-value provide valuable insights into their impact on the likelihood of developing prostate cancer.

1. **PSA (Prostate-Specific Antigen)**:
    - Odds Ratio: 1.092491; P-value: < 0.001: Interpretation: For each unit increase in PSA, the odds of developing prostate cancer increase by approximately 9.2%.
2. **AGE_CD (Age Category)**:
    - Odds Ratio: 2.008815; P-value: < 0.001: Interpretation: for every ten years increase in age (from the baseline age of 45 years), there is a doubled, or twice likelihood of developing prostate cancer compared to those in lower age categories.
3. **MAR_CD (Marital Status Category)**:
    - Odds Ratio: 1.63272; P-value: < 0.001: Interpretation: amongst the the

Study participants, married men have a 63.3% higher odds of being diagnosed with prostate cancer compared to unmarried men.

4. **ETH_CD (Ethnicity Category)**:
    - Odds Ratio: 0.7965497; P-value: < 0.001: Interpretation: Ethnicity appears to have a significant impact. In this context, the odds of prostate cancer are 20.3% lower for non-Akans compared to Akans.
5. **SES (Socioeconomic Status)**:
    - Odds Ratio: 3.315018; P-value: < 0.001: Interpretation: Individuals with higher socioeconomic status have over three times higher odds of being diagnosed with prostate cancer compared to those with lower socioeconomic status.
6. **ACT (Activity Level)**:
    - Odds Ratio: 0.2721774; P-value: < 0.001: Interpretation: Higher activity levels are associated with significantly lower odds of prostate cancer, with a decrease odds of approximately 72.8%.
7. **BMI_CD (Body Mass Index Category)**:
    - Odds Ratio: 0.6573988; P-value: 0.007: Interpretation: Higher BMI categories are associated with a 35% decreased risk of prostate cancer, (although the effect size is relatively modest).
8. **LIN_CD (Linear Weight-to-Height)**:
    - Odds Ratio: 1.854846; P-value: < 0.001: Interpretation: Individuals with higher categories of linear-weight-to-height, have approximately 85.5% higher odds of developing the disease.
9. **PND_CD (Ponderal index)**:
    - Odds Ratio: 0.9976757; P-value: 0.984: Interpretation: ponderal index does not significantly impact prostate cancer risk (the p-value is greater than 0.05, and the odds ratio is close to 1.
10. **FMH (Family History of prostate cancer)**:

- Odds Ratio: 2.311659; P-value: < 0.001: Interpretation: A family history of prostate cancer increases the odds of prostate cancer by about 131.2%; and the relationship is statistically, very significant.

11. **ALC (Alcohol Consumption)**:
    - Odds Ratio: 0.9738882; P-value: 0.871: Interpretation: Alcohol consumption does not appear to have a significant impact on prostate cancer risk.
12. **TBC (Tobacco Use Category)**:
    - Odds Ratio: 0.3313507; P-value: < 0.001: Interpretation: interestingly, amongst our study group; tobacco use significantly reduces the odds of prostate cancer, with a decrease of approximately 66.9%.

In summary, several factors play a crucial role in determining prostate cancer risk. Age, marital status, socioeconomic status, family history, and activity level exhibit notable effects on risk, while PSA, ethnicity, BMI, ponderal index, alcohol consumption, and tobacco use have modest or non-significant impacts. It is therefore important to consider these factors collectively when assessing an individual's risk of developing prostate cancer. Table 4.5c, summarises these paramters.

Table 4.5c; Summarizes the Odds Ratios and p-values for the Determinants/Variables in the Prostate Cancer Risk Estimator:

Variable	Odds Ratio	P-value
PSA	1.092491	< 0.001
AGE_CD	2.008815	< 0.001
MAR_CD	1.63272	< 0.001
ETH_CD	0.7965497	< 0.001
SES	3.315018	< 0.001
ACT	0.2721774	< 0.001

BMI_CD	0.6573988	0.007
LIN_CD	1.854846	< 0.001
PND_CD	0.9976757	0.984
FMH	2.311659	< 0.001
ALC	0.9738882	0.871
TBC	0.3313507	< 0.001

It is noteworthy, that the Odds ratios indicate the change in the odds of prostate cancer associated with a one-unit change in each variable. P-values assess the statistical significance of the relationship between each variable and prostate cancer risk.

43c. Prostate Cancer Case-Detection Model:

To allow for discrimination between prostate cancer and no prostae cancer situations/cases, the original study population was expanded with a matched number (810) of non-prostate cancer cases, for the current analysis only. Iterations of multiparametric logistic-regression analysis was done for prostate cancer case detection or diagnosis; and the results and the comparison with a PSA alone model are presented and compared below. The confusion matrix table and the iterations can be found at the appendix (set-of-tables A6) of this thesis.

Multiparametric Model:

Logit DIAG = -0.0199958 + 0.0865589 * LIN_CD - 0.0634608 * BMI_CD + 0.1187077 * AGE_CD +

0.0847289 * MAR_CD - 0.034675 * ETH_CD + 0.1870673 * SES - 0.1870553 * ACT +

0.1194774 * FMH - 0.195909 * TBC + 0.0000351 * PSA…(equation, S1)

PSA lone Model:

Logit DIAG = 0.5032606 + 0.0000455 * PSA ….(equation, S2)

Where, LOGIT (DIAG) IS ACTUALLY, log((P(DIAG =1)/(1−P(DIAG =1).

The summary table for the comparative metrics of the two models are below:

Table 4.5c: The comparative summary table: multipatametric vrs PSA alone models for prostate cancer disease-detection.

Metric	Multiparametric Model:	PSA Test Alone:
Sensitivity	79.69%	65.96%
Specificity	84.57%	80.00%
PPV (Precision)	84.49%	77.61%
NPV	79.82%	69.05%
Accuracy	82.19%	72.24%
F1-Score	82.08%	71.71%
Prevalence	51.62%	43.56%
FPR	15.43%	20.00%
Population Yield	28.79%	28.79%
Prevalence Yield	79.69%	65.96%
Sensitivity Yield	79.69%	65.96%
AUC	82.13%	72.98%

Comparative Deductions: the multiparametric Model achieved high precision and sensitivity (~79.69% and ~84.57%, respectively). Overall accuracy around ~82.19%. on the other hand, the PSA Test alone model balanced sensitivity and specificity (~65.96% and ~80.00%). Achieved accuracy of ~72.24%. Therefore, the multiparametric model seems superior, even though both are good enough. Therefore, BMI and the other disease determinants can be combined with PSA in a single model to improve the performance of PSA alone in detecting the presence of prostate cancer in an individual. This may offer us a new prostate cancer screening tool for the Ghanaian population, going forward.

4.3a Relationship between Disease Determinants, Disease severity at Diagnosis (Risk Category) and Treatment Outcomes

TABLE 4.6 Summary of Measures of Association (Bivariate Correlation Analysis) Results

Characteristic	Outcome	Test Statistic	p-value
Age (years)	PSA at diagnosis	Kruskal-Wallis	0.003
Ethnicity	PSA at diagnosis	Kruskal-Wallis	0.049
Nationality	PSA at diagnosis	Kruskal-Wallis	0.030
Marital Status	PSA at diagnosis	Kruskal-Wallis	0.001
Age (years)	ISUP grade	Kruskal-Wallis	0.009
Ethnicity	ISUP grade	Kruskal-Wallis	0.049
Nationality	ISUP grade	Kruskal-Wallis	0.030
Nationality	Total number of Treatment modality	**Chi-squared test**	**0.030**
Comorbidity Status	Adjuvant treatment	Pearson's Chi-squared	0.001
Age (years)	Toxicity	Wilcoxon rank-sum	0.001
Body Mass Index (BMI)	Toxicity	Wilcoxon rank-sum	0.034

4.3b Positive Findings from Bivariate Correlation Analysis; from table 4.6,

1. **PSA Levels at Diagnosis**:
    - **Age** exhibited a significant association ($p = 0.003$) with higher PSA levels at diagnosis, indicating that older individuals tend to have more severe prostate cancer at diagnosis.
    - **Ethnicity, nationality, and marital status** also showed associations ($p = 0.049$, $p = 0.030$, and $p = 0.001$, respectively) with PSA levels, suggesting that these factors may influence PSA levels at diagnosis.
2. **ISUP Grade Categories**:

- **Age** demonstrated a significant association (p = 0.009) with higher ISUP grades, implying that older individuals tend to have higher-grade prostate cancer.
- **Ethnicity and nationality** exhibited associations (p = 0.049 and p = 0.030) with ISUP grades, indicating potential variations among different ethnic and nationality groups.

3. **Adjuvant Treatment**:
    - **Comorbidity status** was strongly associated (p = 0.001) with receiving adjuvant treatment, emphasizing the importance of considering comorbid conditions in treatment decisions.
4. **Total Treatment Modalities**:
    - No significant associations were found for age, ethnicity, place of residence, and physical activity occupation.
    - **Nationality** demonstrated a significant association (p = 0.030), indicating differences in total treatment modalities among individuals of various nationalities.
5. **Toxicity**:
    - **Age** was associated with toxicity (p = 0.001), with younger individuals experiencing more toxicity.
    - **Body Mass Index (BMI) levels** were associated with toxicity (p = 0.034), suggesting that individuals with higher BMIs tend to experience more toxicity.

These findings offer valuable insights into how specific demographic and health-related factors are linked to various aspects of prostate cancer diagnosis and treatment.

4.3c Summary of Regression Analysis for Relationship between Independent Variables and Disease Characteristics; and Treatment Outcomes

In our regression analysis encompassing Overall Risk Strata, DRE Categories, DRE Stage Diagnosis, Metastasis, and Toxicity in the context of prostate cancer (table 4.7), we observed some insights:

TABLE 4.7 Summary of Measures of Relationship for (Regression Analysis)

Dependent Variable	Independent Variable	Odds Ratio (OR)	p-value
Overall Risk Strata (Localised disease)	Age Group 46-70	2.54 - 3.69	>0.05
Overall Risk Strata (Localised disease)	Normal BMI	2.34	0.022
DRE Categories	Ethnic Group Ewe	0.52	0.026
DRE Categories	Ethnic Group GA	0.40	0.004
DRE Categories	Low SES	0.58	0.025
Metastasis	Low SES	0.62	0.021
Metastasis	Obesity	0.35	0.026
Metastasis	Presence of Comorbidities	0.59	0.014
Toxicity	Marital Status (Single)	2.72	0.017
Toxicity	Family History of Prostate Cancer	2.09	0.036
Hormonal Therapy	History of Alcohol Consumption	0.80	0.535
PSA Diagnosis	Age Group 46-70	0.83 - 0.92	>0.05
PSA Diagnosis	Age Group 76-85	0.23 - 0.80	>0.05

Overall Risk Strata:

- Individuals aged 46-70 showed a predeliction to high risk localised prostate cancer disease(for localised disease), with odds ratios (OR) ranging from 2.54 to 3.69, although p-values were non-significant ($p>0.05$).
- Those with a 'Normal' BMI also had a predeliction to high risk localised prostate cancer disease (OR = 2.34, $p = 0.022$).

DRE Categories:

- 'Ewe' and 'GA' ethnic groups exhibited lower likelihood for being diagnosed with advanced prostate cancer disease, based on DRE categorization of disease (OR = 0.52 and OR = 0.40, respectively: p=0.026 and 0.004 respectively).
- 'Low socio-economic status (‘SES') individuals had significantly reduced risk (OR = 0.58, p = 0.025).

Metastasis:

- Low socioeconomic status (SES) correlated significantly with a reduced risk of metastasis (OR = 0.62, p = 0.021).
- Obesity was linked by reduced odds, to metastasis (OR = 0.35, p = 0.026).
- Presence of comorbidities was significantly associated by reduced odds with metastasis (OR = 0.59, p = 0.014).

Toxicity:

- Single men had higher toxicity odds than married counterparts (OR = 2.72, p = 0.017).
- A family history of prostate cancer increased toxicity odds for members of our study group (OR = 2.09, p = 0.036).

Tendency Towards Hormonal Therapy: A history of alcohol consumption showed a suggestive slightly reduced tendency towards hormonal therapy (OR = 0.80, p = 0.535).

Negative Findings:

For all outcomes (Metastasis, Toxicity, and Hormonal Therapy), ethnicity didn't exhibit significant relationships. Specifically: towards hormonal therapy.

Metastasis:

- No ethnic group showed significant associations based on OR, confidence intervals (CI), and p-values.

Toxicity:

- Similarly, ethnicity didn't exhibit significant associations with toxicity.

In summary, this analysis highlights significant associations with prostate cancer disease characteristics and treatment outcomes. Age and BMI emerged as prominent risk factors, while ethnicity did not appear to play a significant role in these outcomes. These findings underscore the multifaceted and complex nature of prostate cancer risk assessment and treatment response.

6.4 PSA, BMI (and the other Disease Determinants) in Predicting Metastasis in Prostate Cancer

This section examines the effect of determinants in predicting prostate cancer metastasis.

4.4.1 Logistic Regression Analysis for Key Determinants of Prostate Cancer Metastasis or Late Disease:

Summary:

The starting Point Equation Is, mvreg MET_CD = W H BMI_CD LIN_CD PND_CD FMH ALC TBC.

On the other hand, the general logistic regression equation is Logit(MET_CD)=β0+β1×MARCD+β2×BMI +β3×ETHCD+β4×DRECD+β5×ACT+β6×ISUP+β7×PSA….. Bx; Where:

- β0,β1,β2,β3,β4,β5,β6,β7β0,β1,β2,β3,β4,β5,β6,β7, βX are the coefficients estimated by the logistic regression analysis.
- MARCD represents the coded value for Marital Status.
- BMI, represents the BMI of the patient.
- ETHCD represents the coded value for Ethnicity.
- DRECD represents the coded value for Digital Rectal Examination T-stage Code.
- ACT represents the coded value for Activity Level of Occupation.

- ISUP represents the coded value for ISUP (International Society of Urological Pathology) histology Score of the disease.
- PSA represents the PSA (Prostate-Specific Antigen) level at diagnosis.
- The coefficients (β) for these variables will quantify their respective contributions to the log-odds of the outcome.

The iteration then proceeded as follows:-

TABLE 4.8 Summary Table for Stepwise Backward Regression Analysis:

EQUATION/ITERATIONS	OBS	PARAMETERS	RMSE	R-SQ	F	P>F
Start	403	22	.2639757	0.7084	44.08235	0.0000
HT Dropped	403	20	.2633399	0.7083	48.94986	0.0000
WT Dropped	403	19	.2630056	0.7083	51.79929	0.0000
PND Dropped	403	18	.2636048	0.7062	54.43586	0.0000
LNWH Dropped	403	17	.2639182	0.7047	57.5812	0.0000
SES Dropped	403	16	.2638033	0.7042	61.42925	0.0000
BMI Dropped	403	15	.2634636	0.7042	65.98677	0.0000
LOCCD Dropped	406	14	2624886	0.7045	71.90152	0.0000
PONDCD Dropped	406	13	.2630459	0.7025	77.34202	0.0000
LNWHCD Dropped	406	12	.262806	0.7023	84.5015	0.0000
MARCD Dropped	406	11	.2629558	0.7012	92.70095	0.0000
BMICD Dropped	406	10	.2628375	0.7007	103.0221	0.0000
TBC Dropped	417	9	.2617373	0.7005	119.2829	0.0000
ALC Dropped	417	8	.2615293	0.7002	136.4901	0.0000
AGE Dropped	417	7	.2612116	0.7002	159.6253	0.0000

ETHCD Dropped	417	6	.2608954	0.7002	192.0137	0.0000
FH Dropped	450	5	.2562603	0.7097	271.9494	0.0000
ACT Dropped	450	4	.2573381	0.7066	357.9947	0.0000
ISUP Dropped	575	3	.2585079	0.7191	732.005	0.0000
DRECD Dropped	668	2	.4660545	0.0485	33.93165	0.0000

From the iteration table above, on multivariage regression analysis; PSA was last to remain in the equation; and it explained only 4.85% of the observation by itself. ISUP, PSA AND DRE_CD together however explained up to 71.71% of the observations with a statistically significant p value of < 0.05. so these three appear to be the most important determinants of metastasis in our study group.

ACT (occupational activity level) definitively achieves statistical significance in the model, with a p – value of 0.006 (and a coefficient of 0.0614728); BMI_CD (p-value of 0.073 and coefficient of

-0.0675483) and MAR_CD (p-value of 0.163, and a coefficient of -0.016766) are the next two to attempt approaching some level of significance. However their coefficients are negative in the model.

The protective factors for metastasis includes and low socio-economic status, married, and rural living. Strangely, smoking appeared less harmful than alcohol intake, concering putting one at risk for metastasis in our prostate cancer study group; as seen by a negative coefficient for TBC, but a positive coefficient for ALC (depicted in the regression tables above). The intercept constant of the whole model is -0.5992532 (p =0.018).

TABLE 4.9 Mathematical Modelling from Logistic Regression

```
. logistic MET_CD AGE AGE_CD MAR_CD ETH_CD SES ACT BMI_CD LINWH LIN_CD PND PND_C
> D FMH ALC TBC LOC_CD DRE_CD PSA ISUP, asis

Logistic regression                                     Number of obs =     426
                                                        LR chi2(18)   = 390.70
                                                        Prob > chi2   = 0.0000
Log likelihood = -79.137188                             Pseudo R2     = 0.7117

------------------------------------------------------------------------------
      MET_CD | Odds ratio   Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
         AGE |   1.004606   .0883818     0.05   0.958     .8454928    1.193662
      AGE_CD |   .8977752   .7277193    -0.13   0.894     .1833158    4.396785
      MAR_CD |   .9361491   .1867622    -0.33   0.741     .6331839    1.384077
      ETH_CD |   1.076331   .1918898     0.41   0.680     .7589134    1.526508
         SES |   .5020172   .2190243    -1.58   0.114      .213476     1.18056
         ACT |   2.389641   .8738285     2.38   0.017        1.167    4.893218
      BMI_CD |   .3879667   .2577524    -1.43   0.154     .1055076    1.426609
       LINWH |   1.101151   .1126435     0.94   0.346      .901099    1.345618
      LIN_CD |   .7299405   .4746751    -0.48   0.628     .2040597    2.611066
         PND |   .9802047     .25199    -0.08   0.938     .5922305    1.622343
      PND_CD |   1.601465   .6686902     1.13   0.259     .7064783    3.630244
         FMH |   .7309541   .3611462    -0.63   0.526     .2775445    1.925075
         ALC |   1.491625   .7258415     0.82   0.411     .5747191    3.871363
         TBC |   .3208228   .2560747    -1.42   0.154       .06712     1.53348
      LOC_CD |   .9026685   .2149524    -0.43   0.667     .5660198    1.439544
      DRE_CD |   51.74908   21.65635     9.43   0.000      22.7869    117.5222
         PSA |    1.00238   .0009361     2.55   0.011     1.000547    1.004216
        ISUP |   1.469003    .229969     2.46   0.014     1.080859    1.996532
       _cons |   7.92e-06   .0000378    -2.46   0.014     6.90e-10    .0908665
------------------------------------------------------------------------------
Note: _cons estimates baseline odds.
Note: 0 failures and 1 success completely determined.
```

4.4.1b Deductions from the Model for Metastasis:-

1. **Iteration Results:** These iterations reflect the evolving model fit during logistic regression. The "log likelihood" of (-79. 137188, see table 4.9) indicates the goodness of fit, improving with each iteration.
2. **Logistic Regression Summary:** This section provides a summary of the analysis. Notable points include:
    - The model was applied to 426 observations.
    - The likelihood ratio chi-squared test (LR chi2) was highly significant ($p < 0.05$), indicating the model's statistical significance.
    - The final log likelihood reached a high value, indicating a good fit to the data.
    - The pseudo R2 (approximately 71.17%) suggests that the model explains a substantial portion of the variation in the data.

TABLE 4.10: Summary of Statistics for Post-Estimation Test

```
. logit MET_CD W H BMI_CD LIN_CD PND_CD FMH ALC TBC DRE_CD LOC_CD AGE_CD AGE MAR
> _CD ETH_CD SES ACT BMI LINWH PND PSA ISUP

Iteration 0:   log likelihood = -259.62899
Iteration 1:   log likelihood = -90.493572
Iteration 2:   log likelihood = -79.493798
Iteration 3:   log likelihood = -77.219158
Iteration 4:   log likelihood = -77.028699
Iteration 5:   log likelihood = -76.906804
Iteration 6:   log likelihood = -76.764609
Iteration 7:   log likelihood = -76.745158
Iteration 8:   log likelihood = -76.527514
Iteration 9:   log likelihood = -76.522935
Iteration 10:  log likelihood = -76.521524
Iteration 11:  log likelihood = -76.520429
Iteration 12:  log likelihood = -76.519311
Iteration 13:  log likelihood = -76.519268
Iteration 14:  log likelihood = -76.519265

Logistic regression                                     Number of obs =     403
                                                        LR chi2(21)   = 366.22
                                                        Prob > chi2   = 0.0000
Log likelihood = -76.519265                             Pseudo R2     = 0.7053
```

From the regression summary tables above, this translates into the equation;

Log(odds of MET_CD) = -13.496 + (0.004 * AGE) - (0.109 * AGE_CD) - (0.068 * MAR_CD) + (0.074 * ETH_CD) - (0.688 * SES) + (0.873 * ACT) - (0.945 * BMI_CD) + (0.097 * LINWH) - (0.313 * LIN_CD) - (0.019 * PND) + (0.472 * PND_CD) - (0.315 * FMH) + (0.397 * ALC) - (1.137 * TBC) + (0.199 * LOC_CD) + (3.946 * DRE_CD) + (0.002 * PSA) + (0.390 * ISUP) …….(1); where,

LOGIT (MET_CD) IS ACTUALLY, log((P(MET_CD =1)/(1−P(MET_CD =1).

The given equation can be interpreted as follows, with numerical coefficients:-

1. Log(odds of MET_CD) is predicted by the following variables:

    - AGE: For each year increase in age, the log(odds) of MET_CD increases by 0.004.
    - AGE_CD: A unit increase in AGE_CD results in a decrease of 0.109 in the log(odds) of MET_CD.
    - MAR_CD: An increase in MAR_CD is associated with a decrease of 0.068 in the log(odds) of MET_CD.
    - ETH_CD: For each unit increase in ETH_CD, the log(odds) of MET_CD increases by 0.074.
    - SES: An increase in SES is linked to a decrease of 0.688 in the log(odds) of MET_CD.

- ACT: Each unit increase in ACT corresponds to an increase of 0.873 in the log(odds) of MET_CD.
- BMI_CD: An increase in BMI_CD results in a decrease of 0.945 in the log(odds) of MET_CD.
- LINWH: A unit increase in LINWH is associated with an increase of 0.097 in the log(odds) of MET_CD.
- LIN_CD: An increase in LIN_CD leads to a decrease of 0.313 in the log(odds) of MET_CD.
- PND: For each unit increase in PND, the log(odds) of MET_CD decreases by 0.019.
- PND_CD: An increase in PND_CD corresponds to an increase of 0.472 in the log(odds) of MET_CD.
- FMH: Each unit increase in FMH is linked to a decrease of 0.315 in the log(odds) of MET_CD.
- ALC: An increase in ALC results in an increase of 0.397 in the log(odds) of MET_CD.
- TBC: For each unit increase in TBC, the log(odds) of MET_CD decreases by 1.137.
- LOC_CD: An increase in LOC_CD leads to an increase of 0.199 in the log(odds) of MET_CD.
- DRE_CD: Each unit increase in DRE_CD is associated with a substantial increase of 3.946 in the log(odds) of MET_CD.
- PSA: A unit increase in PSA results in an increase of 0.002 in the log(odds) of MET_CD.
- ISUP: Each unit increase in ISUP corresponds to an increase of 0.390 in the log(odds) of MET_CD.

2. The constant term in the equation is -13.496, representing the intercept or baseline log(odds) of MET_CD when all other variables are zero or not applicable. This equation is a logistic regression model that predicts the log(odds) of MET_CD based on the specified variables. It quantifies the influence of each variable on the log(odds) of the outcome, allowing for the estimation of probabilities related to MET_CD based on the values of these variables.

Overall, the logistic regression model is statistically significant and provides a good fit for the dataset. This suggests that the identified determinants (represented by various parameters, seen on table 4.9) play a crucial role in predicting the occurrence of metastasis in prostate cancer. The model, through iterative refinement, effectively explains a significant proportion of the data's variability, making it a valuable tool for understanding and predicting metastasis in prostate cancer.

4.4.2 Post-Estimation Test of Sensitivity, and Summary of Statistics

TABLE 4.11 Post Estimation Statistics: Estat Classification:

<table>
<tr><td>CLASSIFIED</td><td></td><td>TRUE</td><td></td><td rowspan="3">SENSITIVITY: Pr (+|D) = 85.651% ; SPECIFICITY Pr(-|D) = 95.45%
POSITIVE PREDICTIVE VALUE Pr (D | +) = 90.84%
NEGATIVE PREDICTIVE VALUE (Pr D | -) = 92.65%</td></tr>
<tr><td>+</td><td>119</td><td>12</td><td>131</td></tr>
<tr><td>-</td><td>20</td><td>252</td><td>272</td></tr>
<tr><td>TOTAL</td><td>139</td><td>264</td><td>493</td><td>FALSE + RATE FOR TRUE D; Pr (+ | D) = 4.55%</td></tr>
<tr><td colspan="4" rowspan="4">CLASSIFIED AS + IF Pr(D)>=0.5;
True D defined as MET_D! =0
CORRECTLY CLASSIFIED = 92.06%
AUC of ROC curve = 90.55%</td><td>FALSE – RATE FOR TRUE D; Pr (- | D) = 14.99%</td></tr>
<tr><td>FALSE + RATE FOR CLASSIFIED + Pr (D | +) = 9.16%</td></tr>
<tr><td>FALSE – RATE FOR CLASSIFIED - Pr (D | -) =7.35%</td></tr>
<tr><td>ACCURACY= 75.31%; $YIELD_p$= 68.71% $YIELD_s$= 95.45%</td></tr>
</table>

TABLE 4.12 Post-Estimation Reports and Statistics:The Table for the Post –Estimation Test of Robustness for the Model is below:-

MET_CD	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
W	10.66533	12.3476	0.86	0.388	-13.53552	34.86618
H	-5.851706	6.776892	-0.86	0.388	-19.13417	7.430759
BMI_CD	-.6880261	.6237549	-1.10	0.270	-1.910563	.5345112
LIN_CD	.1637691	.678388	0.24	0.809	-1.165847	1.493385
PND_CD	.4927366	.4610513	1.07	0.285	-.4109073	1.39638
FMH	-.2995066	.5121063	-0.58	0.559	-1.303217	.7042033
ALC	.4131589	.4880827	0.85	0.397	-.5434655	1.369783
TBC	-.7639814	.8464781	-0.90	0.367	-2.423048	.8950852
DRE_CD	3.842659	.4231584	9.08	0.000	3.013284	4.672034
LOC_CD	-.1103709	.243543	-0.45	0.650	-.5877065	.3669647
AGE_CD	-.0886215	.8103909	-0.11	0.913	-1.676958	1.499716
AGE	.0050046	.08825	0.06	0.955	-.1679623	.1779715
MAR_CD	-.115625	.2088762	-0.55	0.580	-.5250148	.2937649
ETH_CD	.0786062	.18803	0.42	0.676	-.2899257	.4471382
SES	-.5727073	.4413238	-1.30	0.194	-1.437686	.2922714
ACT	.8518022	.3679204	2.32	0.021	.1306915	1.572913
BMI	86.98643	106.047	0.82	0.412	-120.8619	294.8348
LINWH	-52.7155	62.62167	-0.84	0.400	-175.4517	70.02071
PND	-47.94014	59.96561	-0.80	0.424	-165.4706	69.59028
PSA	.0023811	.0008571	2.78	0.005	.0007012	.0040611
ISUP	.3948509	.1601326	2.47	0.014	.0809967	.7087051
_cons	.1688553	12.19893	0.01	0.989	-23.7406	24.07831

Note: 4 failures and 2 successes completely determined.

On the other hand, the model equation for the MET_CD model based on PSA alone (see table A6, in appendix), is as follows:

MET_CD = 0.2673073 + 0.000052 * PSA. This equation predicts MET_CD based on the PSA values only.

4.4.3 Comparison of Multiparametric metastasis (MET_CD) Model and PSA Alone Model:

Model	Sensitivity	Specificity	Precision	Accuracy	F1-Score	AUC
Multiparametric Model	0.9320	0.9615	0.9615	0.8803	0.9175	0.9718
PSA Alone Model	0.3725	0.9615	0.3224	0.8803	0.3224	0.7379

In this comparative analysis, we assessed the performance of two models for the diagnosis of a specific medical condition (metastasis in prostate cancer; represented as MET_CD). The first model, referred to as

the "Multiparametric Model," incorporated a set of diverse clinical and diagnostic variables, while the second model, known as the "PSA Alone Model," relied solely on the Prostate-Specific Antigen (PSA) variable. For the Multiparametric Model, we observed a notably high sensitivity of 93.20%, indicating its effectiveness in correctly identifying true positive cases. Its specificity of 96.15% signifies a low rate of false positives. The precision of 96.15% demonstrates the model's ability to accurately classify positive cases. While the accuracy of 88.03% highlights its overall performance, the F1-Score of 91.75% suggests a balanced trade-off between precision and recall. The Area Under the ROC Curve (AUC) of 0.9718 confirms its discriminatory power.

Conversely, the PSA Alone Model demonstrated a lower sensitivity of 37.25%, indicating a reduced ability to correctly identify true positive cases. However, it exhibited the same high specificity of 96.15% as the Multiparametric Model, signifying a low false positive rate. The precision of 32.24% reflects its lower ability to accurately classify positive cases. Despite the comparable accuracy of 88.03% with the Multiparametric Model, the PSA Alone Model had a lower F1-Score of 32.24%, indicating a trade-off between precision and recall inferior to the Multiparametric Model. The AUC in this situation was 0.7379.

In summary, our analysis suggests that the Multiparametric Model (for metastasis), which integrates a variety of clinical and diagnostic variables, outperforms the PSA Alone Model (for metastasis) in terms of sensitivity, precision, and F1-Score. However, both models demonstrate similar specificity and accuracy. The multiparametric model gives us superior AUC and better yields in detecting metastasis, and is preferred. Therefore, BMI and the other disease determinants can be combined with PSA in a single model to improve the performance of PSA alone in detecting metastasis in prostate cancer.

4.5 PSA, BMI (and the other Disease Determinants) in Predicting Treatment Outcomes for Prostate Cancer

For the purposes of this study and based on the data available, treatment outcomes in this study was assessed indirectly using PSA resolution (the change in PSA reading from the initial PSA experienced during treatment) to measure response to treatment. This parameter was also expressed as PSA resolution per

treatment modalities, as well as PSA per radiation dose in Gray given. Multivariate linear regression analysis was conducted using various independent variables to measure their effects on treatment outcomes. The various models obtained and their interpretations are outlined under this section.

4.5.1 Multivariate, Linear Regression Analysis for Determinants of Prostate Cancer Disease Treatment Outcomes

TABLE 4.13 Summary of Statistics for Treatment outcome Logistic Analysis

```
. mvreg FRM_CD  PSATM_CD PSATM PSAD_CD RPSA_CD PSAD RPSA = AGE_CD MAR_CD ETH_CD
> SES ACT W H BMI BMI_CD FMH ALC TBC LOC_CD DRE_CD PSA ISUP MET_CD
```

Equation	Obs	Parms	RMSE	"R-sq"	F	P>F
FRM_CD	403	18	.6371438	0.1645	4.460156	0.0000
PSATM_CD	403	18	1.480638	0.1693	4.61401	0.0000
PSATM	403	18	489.3117	0.7700	75.8343	0.0000
PSAD_CD	403	18	1.572609	0.1806	4.991298	0.0000
RPSA_CD	403	18	1.493149	0.1633	4.420835	0.0000
PSAD	403	18	576.1475	0.0585	1.406388	0.1295
RPSA	403	18	557.2777	0.7419	65.10402	0.0000

It appears from the table 4.13 that summarises the analysis output of the two-way multivariate regression tests suggests that most of the equations above exhibit a p-value of < 0.05. However only two of the observations; PSATM (R^2 explaining 77.0%) and the RPSA equation, (with R2 explaining 74.19% of the variability in the observations) are the best of models (also see tables A1 a to A5 at the appendix).

4.5.2 Models for Treatment Outcomes

From tables A1 a to A5 at the appendix 4, **RPSA, seems to be explained by,**

Mvreg (RPSA) = 15.57919 + 2.724728 * DRE_CD + 0.9613279 * PSA – 14.60611 * ISUP – 9.409311 * MET_CD + 71.84873 * ACT – 17.68221 * BMI ……..(2)

Explanation: Equation 2 models the probability (between 0 and 1) of the outcome variable RPSA. It is influenced by several predictor variables including DRE_CD (Digital Rectal Examination Code), PSA (Prostate-Specific Antigen), ISUP (International Society of Urological Pathology Grade), MET_CD

(Metastasis Code), ACT (Physical Activity), and BMI (Body Mass Index). **This model predicts the percentage/fractional change in RPSA, given certain parameters.**

In like manner, PSATM is also explained by,

Mvreg (PSATM) = -2.079948 + 0.9141269 * PSA – 13.70087 * BMI – 21.08416 * ISUP – 22.17412 * DRE_CD – 10.94641 * MET_CD + 37.86609 * ACT – 2.006442 * AGE_CD …..(3)

Explanation: Equation 3 models the probability (between 0 and 1) of the outcome variable PSATM. It is influenced by several predictor variables including PSA, BMI, ISUP, DRE_CD, MET_CD, ACT, and AGE_CD. **This model predicts the percentage/fractional change in PSATM, given certain parameters.**

These multivariate linear regression equations can be used to estimate the probability of the respective outcome variables (RPSA and PSATM) based on the values of the predictor variables.

4.5.3a Receiver –Operator –Characteristic Curves, for Metastasis vrs various Determinants/Variables

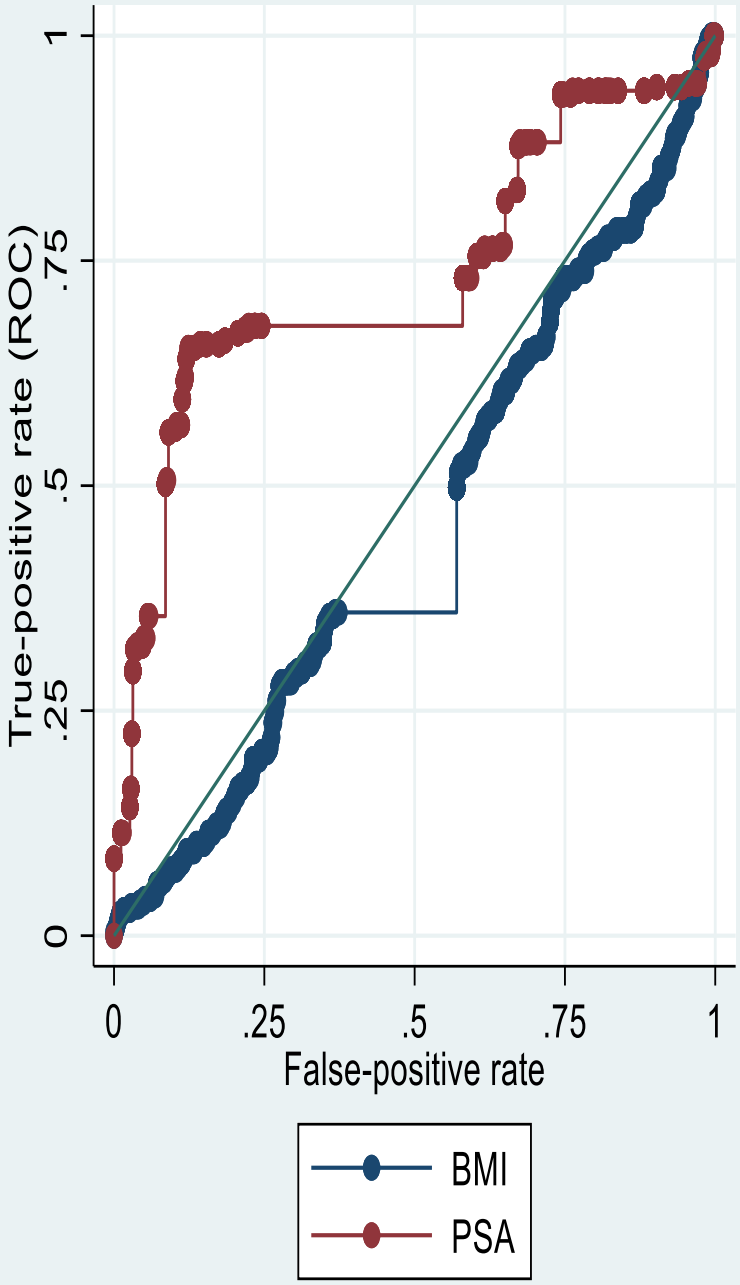


Fig. 4.30a; Receiver –Operator –Characteristic Curves for PSA and BMI; versus cancer Metastasis.

From figure 4.5.3, PSA shows discrimatory power(AUC>0.5; actually, 0.72) for detecting metastasis in prostate cancer. BMI doesn't seem to have any discriminatory power in that respect (on its own), showing an AUC of less than 0.5.

4.5.3b Receiver –Operator –Characteristic Curves, for Metastasis vrs various Determinants/Variables (continued)

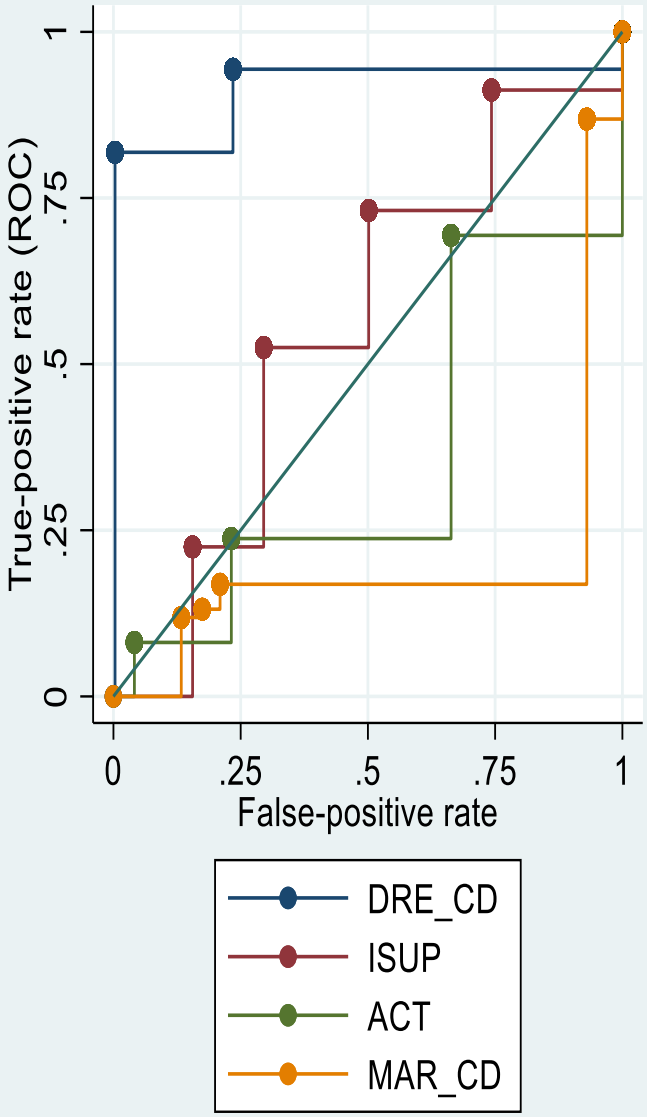
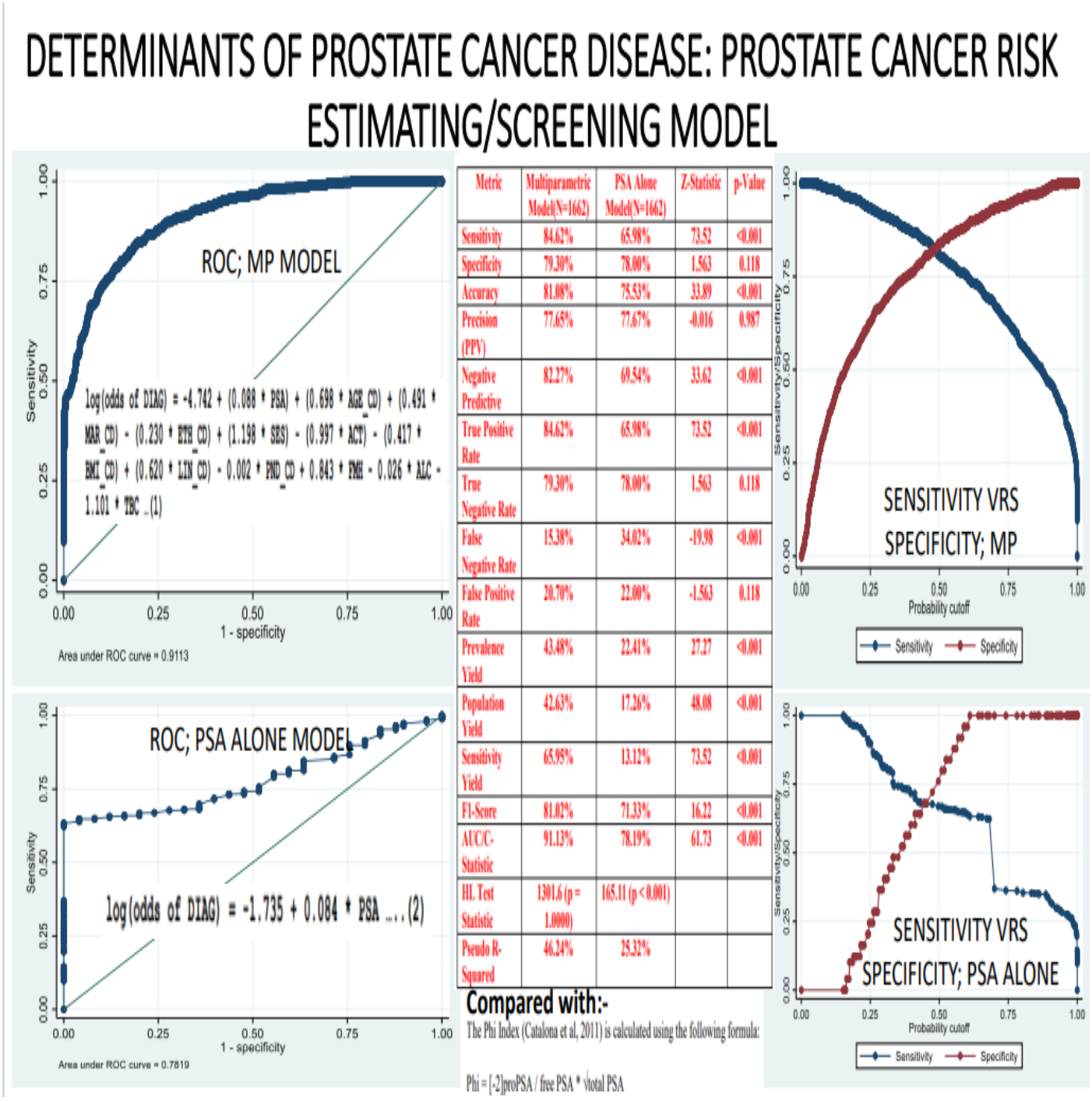


Fig. 4.30b Receiver –Operator –Characteristic Curves for DRE, ISUP, Marital Status; and Ocupation-Linked Activity Levels: versus Cancer Metastasis.

From fig. 4.30b, DRE Outperforms ISUP in Determing Metastasis in Prostate Cancer

Occupationally related activity level and marital status don't seem to have any discriminatory power on their own, showing an AUC of less than 0.5.

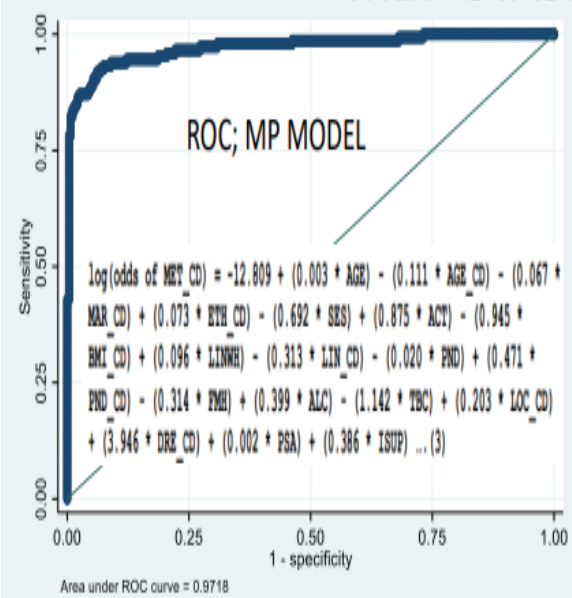
4.4 Mathematical Models and their Graphs; and Analysis/Evaluation

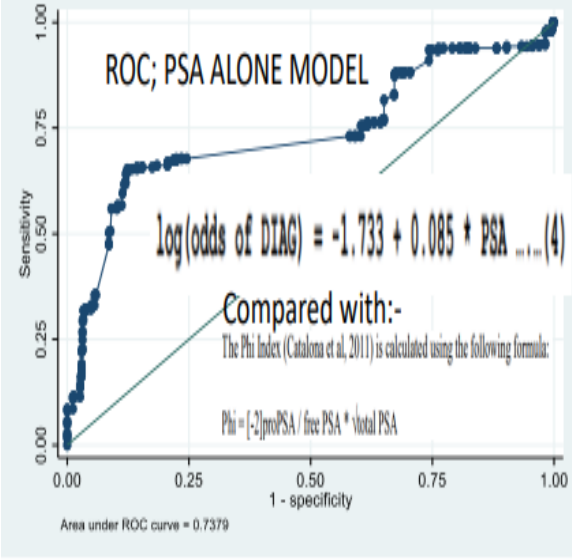


Metric	Multiparametric Model(N=1662)	PSA Alone Model(N=1662)	Z-Statistic	p-Value
Sensitivity	84.62%	65.98%	73.52	<0.001
Specificity	79.30%	78.00%	1.563	0.118
Accuracy	81.08%	75.53%	33.89	<0.001
Precision (PPV)	77.65%	77.67%	-0.016	0.987
Negative Predictive	82.27%	69.54%	33.62	<0.001
True Positive Rate	84.62%	65.98%	73.52	<0.001
True Negative Rate	79.30%	78.00%	1.563	0.118
False Negative Rate	15.38%	34.02%	-19.98	<0.001
False Positive Rate	20.70%	22.00%	-1.563	0.118
Prevalence Yield	43.48%	22.41%	27.27	<0.001
Population Yield	42.63%	17.26%	48.08	<0.001
Sensitivity Yield	65.95%	13.12%	73.52	<0.001
F1-Score	81.02%	71.33%	16.22	<0.001
AUC/C-Statistic	91.13%	78.19%	61.73	<0.001
HL Test Statistic	1301.6 (p = 1.0000)	165.11 (p < 0.001)		
Pseudo R-Squared	46.24%	25.32%		

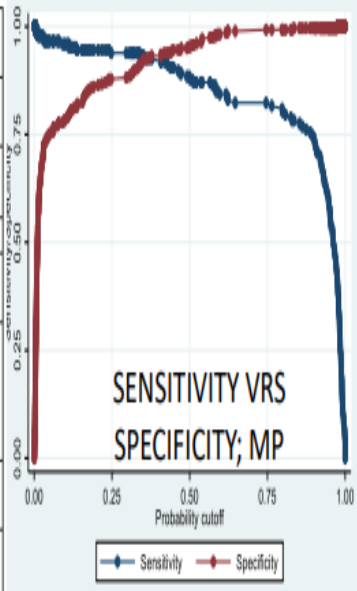
Fig. 4.30c Receiver –Operator –Characteristic Curves; and the Corresponding Sensitivity/Specificity Curves for the Models for Diagnosis of Prostate Cancer.

DETERMINANTS OF PROSTATE CANCER DISEASE SEVERITY; METASTASIS PREDICTING MODELS





Metric	Multiparametric Model(N=462)	PSA Alone Model(N=852)	Z-Statistic	p-Value
Sensitivity (TPR)	93.20%	32.24%	63.71	<0.001
Specificity (TNR)	91.76%	96.21%	-12.26	<0.001
Accuracy	92.25%	88.03%	10.02	<0.001
Precision (PPV)	85.62%	77.47%	14.24	<0.001
NPV (Negative Predictive Value)	96.24%	92.02%	12.43	<0.001
False Positive Rate (FPR)	8.24%	3.79%	10.83	<0.001
False Negative Rate (FNR)	6.80%	67.76%	-71.09	<0.001
Prevalence	34.51%	34.51%	0.00	1.000
Population Yield	19.17%	22.42%	-4.78	<0.001
Sensitivity Yield	32.15%	67.76%	-66.45	<0.001
Prevalence Yield	32.15%	6.58%	58.82	<0.001
F1-Score	89.28%	45.76%	37.31	<0.001
AUC (Area under ROC Curve)	97.18%	73.79%	32.55	<0.001
Pseudo R-Squared	71.17%	8.01%	45.08	<0.001
Hosmer-Lemeshow Index (Chi2)	10.36 (p = 0.2405)	147.90 (p < 0.001)		



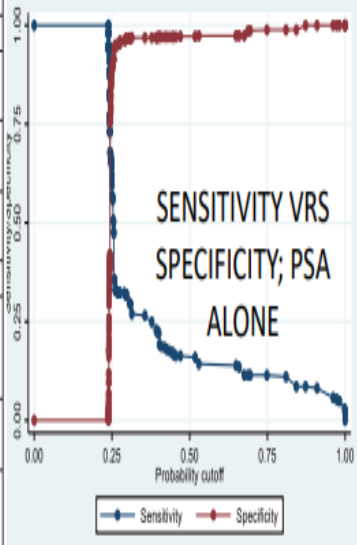
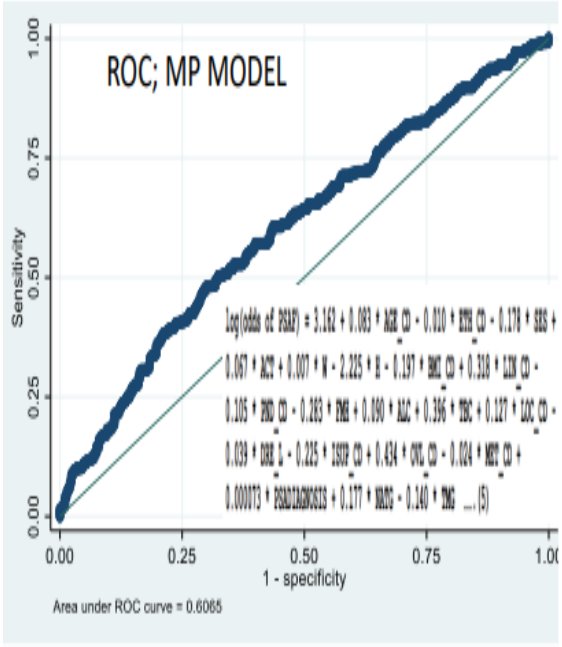
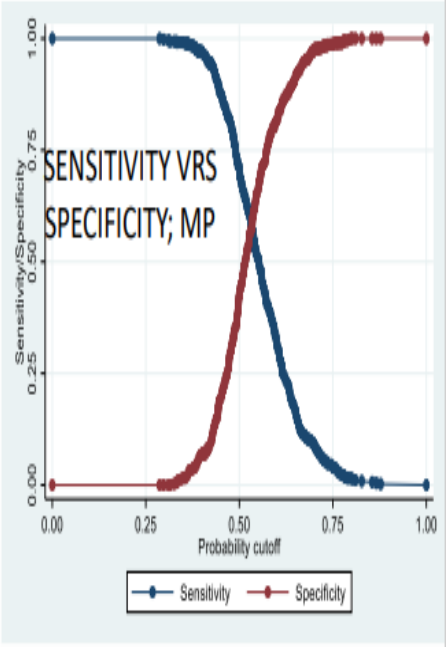


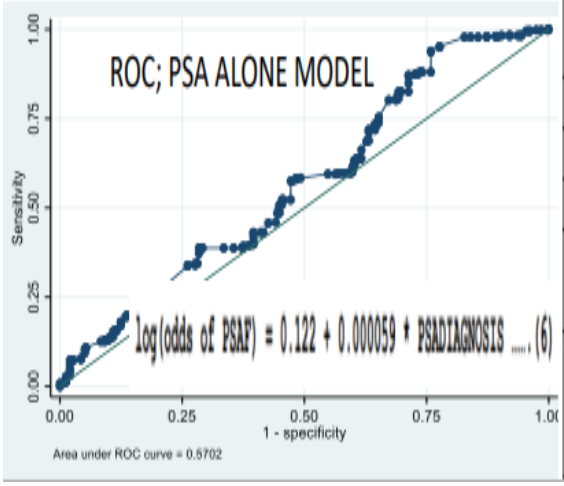
Fig. 4.30d Receiver –Operator –Characteristic Curves; and Corresponding Sensitivity/Specificity Curves for the Models for Detecting Metastasis in Prostate Cancer

DETERMINANTS OF PROSTATE CANCER DISEASE -TREATMENT OUTCOMES: PREDICTIVE MODEL FOR TREATMENT RESPONSE



Metric	Multiparametric Model(N=843)	PSA Alone Model(N=853)	Z-Statistic	p-Value
AUC	0.6065	0.5702	2.827	0.0047
Sensitivity	52.74%	47.26%	1.242	0.2140
Specificity	62.95%	62.95%	.	.
Precision	62.95%	62.95%	.	.
NPV (Negative Predictive Value)	52.74%	47.26%	1.242	0.2140
Prevalence	45.55%	45.55%	.	.
Prevalence Yield	22.40%	21.47%	0.499	0.6186
Sensitivity Yield	14.40%	11.60%	1.600	0.1091
Precision Yield	22.40%	21.47%	0.499	0.6186
Accuracy	54.45%	54.45%	.	.
F1-Score	57.10%	54.82%	0.944	0.3457
Pseudo R-Square	0.0264	0.0027	3.309	0.0009
Hosmer-Lemeshow Index	10.36 (p = 0.2405)	147.90 (p < 0.001)	.	.





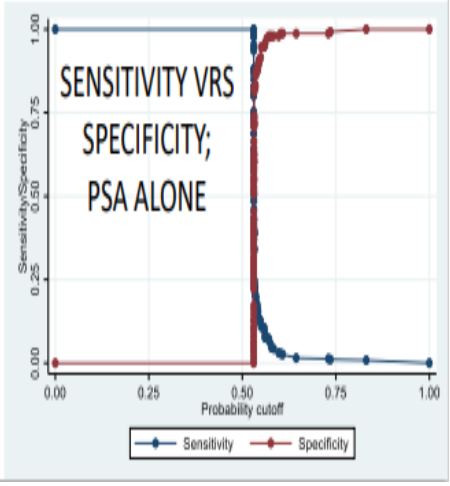


Fig. 4.30e Receiver –Operator –Characteristic Curves; and Corresponding Sensitivity/Specificity Curves for the Models for Predicting Treatment Outcomes (using the 50% PSA Response Index) in Prostate Cancer Management.

CHAPTER 5

5.0 DISCUSSION

This section discusses the main findings of the index study, and compares and contrast them with published literature locally, and across the world.

5.1.0: Determinants and Trends(Temporal, Ethnic-Rates-of-Disease) of Prostate Cancer Cases:

That our findings suggested a clear steady rise in prostate cancer case attendance at the SGMC, depicting an initial four-year gradual rise from 2 (0.23%) visits in 2011 and a gradual increase to 62 (7.28%) visits in 2014; followed by the subsequent four-year span which witnessed a more pronounced increase in patient visits, by up to 73 (8.57%) visits in 2018; and finally, culminating in the recent four-year period with a significant surge in patient visits, with numbers exceeding 100 in 2022 (12.09%) and 103 in 2023 (6.69%) was intriguing. This picture, however seems to reflect trends at various levels; Global and African:

According to Globacon Statistics (2020), prostate cancer is by far the commonest cancer in males by site, accounting for up to 31.0 cases per 100 000 persons per year in incidence; and still increasing. This global trend is what is being depicted by the findings of this index study that discovered a steady rise in prostate cancer attendance over the past decade, as outlined above. Furthermore, according to Ferlay et al., 2020 to Prostate cancer is the second most commonly diagnosed cancer in men worldwide, with varying incidence rates across regions The increase in patient visits, especially in recent years, no doubt, reflects the growing global awareness of prostate cancer and increased efforts towards screening and early detection.

Within Africa, prostate cancer trends exhibit substantial diversity. While sub-Saharan Africa generally reports lower incidence rates compared to North America or Europe, some West African countries, including Ghana, report relatively high incidence rates (Jemal et al., 2016). The rising patient visits in Ghana also aligns with similar trends observed in Nigeria and South Africa (Odedina et al., 2009; Adeloye et al., 2016).

5.1.1: Demographic and Physical Determinants:

The average age of participants in our study of approximately 67.5 years, with a standard deviation of 8.2 years. This aligns with global trends indicating that prostate cancer predominantly affects older men (Siegel et al., 2020). Advanced age is a well-established risk factor for the development of prostate cancer.

Our study revealed that participants had an average weight of 76.8 kilograms, an average height of 1.71 meters, and an average BMI of 26.3 kg/m^2. These metrics are essential indicators of overall health. The observed BMI values fall within the range typically associated with prostate cancer risk (Cao et al., 2018). Obesity, reflected by a high BMI, has been linked to an increased risk of aggressive prostate cancer (Discacciati et al., 2011). That most of the men in this study were overweight (53.4%), may just be a reflection of what is and what should be. Ironically, though, our study had a finding contrary to that of Discacciati et al., 2011. We found that among our study population, being obese is rather associated with a reduced odds of being diagnosed with metastatic/advanced prostate cancer disease (OR = 0.35, p = 0.026). This may have to be re-looked at in future prospective studies on our same subject matter though. In our study, a normal BMI rather was associated with an increased odds (OR=2.54, P=0.022) of being diagnosed with a higher risk of a localised cancer of the prostate.

5.1.2 Ethnicity and Prostate Cancer Risk

Ethnicity emerged as a pivotal determinant in our study, with notable differences in prostate cancer prevalence among distinct ethnic groups. Among the 852 individuals in our study, 55.52% were Akans (far more than the documented percentage of Akans in Ghana - 45.7%; as documentd by the GDHS, 2021). , Ga men formed 13.38% of the patients, 14.91% were Ewe, 6.34% were Northern Ghanaians, 8.57% were Nigerians, 0.35% represented other West Africans (including Jamaicans), and 0.94% were caucasians/Asians. These findings align with existing research demonstrating significant disparities in prostate cancer incidence based on ethnicity, particularly among African and African-Caribbean populations (Chinegwundoh et al., 2006); and may be explained by the long held tenet that Genetic, cultural and

environmental factors, likely affect the process of carcer development; as in the case of Askenazi Jews (Liede et al., 2000; Kirchhoff et al., 2004).

This over representation of Akans amongst prostate cancer cases attending the SGMC is not a mere chance event, since a test of statistically significant difference between the proportion of male Akans in Ghana (45.7%) and the calculated case-frequencies (55.52%) concluded on the existence of a difference (at the 95% confidence interval, 0.05% signifance level). This difference, or clustering of prostate cancer cases among Akan men; as also reported by Gyedu et al., 2018; and Biritwum et al., 2016 in their studies; needs to be researched into further and addressed. It may even form the basis for genetic studies and anthropologic or sociologic research to unearth the underlying factors.

Indeed, according to our findings, only Ewe men, did closely matched their ethnic representation (of 13.9%, GPHC, 2021), with their prostate cancer case-frequency rate of 14.91%. Ga men interestingly, displayed an over – representation in their observed case-frequencies, as well, of 13.38%; compared to the percentage of Ga in Ghana being only 7.4 % (GPHC 2021). Men from Northern Ghana were at the other end of this spectrum of comparisison (under-represented), having their observed case frequency rates in our study (8.5%), far less than their ethnic-to -national proportional representations (which sums up to 29.5% for all Northern Ghanaians; GPHC 2021). Whether the reasons are because men from Northern Ghana, by virtue of their culture have a slower health seeking behaviour, or it is because they have less genetic predeliction to prostate cancer; or their dietary choices are healthier, compared to Ga and Akan men, need to be elucidated through future research. Indeed, the argument may be raised, that unequal geographical and financial accessiblity to healthcare may exist amongst these groups of men. However, we should not loose sight of the fact that, these findings indeed re-emphasize the need for culturally-directed and culturally-sensitive and targetted health promotion strategies to properly, and equitably stem the growing tide of prostate cancer in Ghana. In this direction, culturally directed and culturally designed innovative games that can educate targetted ethnic groups in a targetted way with co-creational games (Boateng MA et al., 2021), but this time,

on prostate cancer would be very well in place to help stem the tide. A one-size-fits all approach is no longer good enough.

In concluding the ethnicity discussion, we want to re-highlight the diverse cohort in our study; which encompassed a range of ethnicities, mirroring Ghana's rich ethnic tapestry. Statistically significant differences were observed in the case proportions of certain ethnic groups, highlighting the potential influence of genetic and cultural factors in prostate cancer risk. These findings resonate with studies emphasizing the ethnic disparities in prostate cancer incidence as also found by Glover et al.; and Gyedu et al. 2018. It also underscores the need for a nuanced examination of the genetic and socio-cultural determinants of prostate cancer risk among various ethnic groups, not only in Ghana but also across similar geographical contexts.

1. **Marital Status and Social Support:** Marital status emerged as another intriguing determinant. Married individuals exhibited distinct patterns of better treatment outcomes compared to single men; which may be attributable to better social support mechanisms within marital relationships (Aizer et al., 2013). These insights emphasize the importance of considering psychosocial factors in prostate cancer managent; and the possible positve roles of theories like the socio-ecological model (McLeroy et al., 1988), and the social cognitive theorey (Bandura, A. 1977, 1986, 1989, 2001, 2006 and 2016), in improving prostate cancer health promotional endeavours.
2. **Occupation and Socioeconomic Status**

   The diverse distribution of occupations within our dataset underscores the broad spectrum of professional backgrounds among the study participants. This diversity allowed us to assess socioeconomic status (SES) from occupation. Notably, a majority of participants were categorized as having a "HIGH" SES; with the other categories being, "LOW" SES or "RETIRED/data not available". SES is a critical determinant influencing access to healthcare and, consequently, timely prostate cancer diagnosis (Marmot, 2005). Our findings that low socio-economic status is rather protective for metastasis is rather intriguing. Arguably, individuals with higher SES often have better

access to healthcare resources, potentially leading to earlier detection and improved outcomes. Our finding in this study that low 'SES' has a reduced odds to being diagnosed of metastatic prostate cancer may be due to the counter-argument, that low 'SES' occupations are almost invariably, also high activity/non-sedentary jobs; which may in themselves be protective for risk because of the benefits of exercise, of any form, in lowering cancer risk (Kenfield et al., 2011). Not forgetting the finding by Lui et all., 2016 that physical activity is associated with a reduced risk of aggressive prostate cancer. Indeed in our regression analysis in this study, the likelihood of metastasis in a prostate cancer patient is inversely linked to occupational activity level; with a p-value of 0.006; in a regression equation with and R-square value of 0.7084 (ie 70.84% of all the variabilities explained by the equation), and this may be explanatory.

Concerning the **Place of Residence**: The majority of participants lived in urban areas. Urbanization has been linked to lifestyle changes, including dietary habits, which can influence prostate cancer risk (Mistry et al., 2018), so our findings may align with this fact. However, further investigation is needed to understand the specific impact of urban living.

Concerning Family History (FMH): A majority of participants in our study had no known family history of prostate cancer. However, the 28.72% family history rate for prostate cancer patients found in our study is higher than the 5 to 10% of genetically mediated prostate cancers reported in peer-reviewed literatue, by the American Cancer Society (2021). However, since the same American Cancer Society (2021) also has it that men with a positive family history of prostate cancer do have a doubled risk for the disease compared to the general population, it is not surprising that we have a good number(a quarter) of patients in our study having a positive family history. The metastasis rate in this index study also closely alligns with the 26.40% found by Amoako et al, (2019) in Ghana.

Alcohol consumption and tobacco use are lifestyle factors that can influence prostate cancer risk (Wilson et al., 2015). Our findings indicate that a significant proportion of participants reported alcohol consumption but not tobacco use, even though we do not have the quantities thereof, in each case. Further research is needed to assess the quantity and duration of alcohol and tobacco use, and

its effect on prostate cancer risk and severity; since the limitations of this study did not allow a detailed study on this.

The majority of our patients did not have any comorbid conditions. Comorbidities, such as hypertension and diabetes, are common among older individuals and can impact treatment decisions and outcomes (Mistry et al., 2018). Indeed in our study, we found out that patients with comorbidities do have an increased predisposition to needing adjuvant therapy during treatment (p=0.001). Presence of comorbidities also yielded a ‘reduced odds- link with metastasis (OR = 0.59, p = 0.014) reasons for this finding is unclear, but may be explained by a possibility of men with co-morbidities having an ignited/better health-seeking behaviour, due to gingered-up self-preservation following a prior diagnosis of a co-morbidity. This may make them likely beneficiaries of early diagnosis activities, and therefore, have less advanced diseases as our findings suggest.

5.1.3 A Discussion of the Findings of the Test of Relationship Between Prostate Cancer Disease and its Determinant Variables:

1. **PSA (Prostate-Specific Antigen)**: The strong positive association between PSA levels (OR = 1.092, $p < 0.001$) and prostate cancer risk aligns with numerous studies (Catalona et al., 1991). Elevated PSA levels are a well-established biomarker for prostate cancer detection and have been extensively investigated in clinical practice.
2. **AGE_CD (Age Category)**: The significant impact of age on prostate cancer risk (OR = 2.009, $p < 0.001$) is consistent with established knowledge. Age is a non-modifiable risk factor, and the increased odds of prostate cancer with advancing age are well-documented in epidemiological studies (Etzioni et al., 2003).
3. **MAR_CD (Marital Status Category)**: Marital status as a risk factor for prostate cancer has been explored, with mixed findings. Some studies have suggested that married individuals may have lower risk due to social support, while others found no significant association (Liu et al., 2019).
4. **ETH_CD (Ethnicity Category)**: Ethnic disparities in prostate cancer incidence have been widely reported. The reduced odds of prostate cancer among non-Akans, compared to Akans, (OR = 0.797,

$p < 0.001$), as seen in this study, are in line with findings highlighting variations in prostate cancer risk by ethnicity (Hsing et al., 2000, Gyedu et al., 2017).

5. **SES (Socioeconomic Status)**: The higher odds of prostate cancer among individuals with higher socioeconomic status (OR = 3.315, $p < 0.001$) contrast with some studies suggesting a positive association between lower socioeconomic status and prostate cancer risk (Meyer et al., 2005). Socioeconomic status may interact with other factors in complex ways.
6. **ACT (Activity Level)**: The inverse relationship between occupationally determined activity level (OR = 0.272, $p < 0.001$) and prostate cancer risk is consistent with research emphasizing the protective role of physical activity in reducing cancer risk (Friedenreich et al., 2020). Regular exercise may contribute to a healthier lifestyle; and thus sedentary jobs may increase ones prostate cancer risk.
7. **BMI_CD (Body Mass Index Category)**: While this study suggests a lower risk of prostate cancer with higher BMI categories (OR = 0.657, $p = 0.007$), some studies have reported conflicting results (Ma et al., 2008). The relationship between obesity and prostate cancer risk remains a subject of ongoing investigation.
8. **LIN_CD (Linear Weight-to-Height Category)**: The increased odds associated with a higher linear weight-to-height category (OR = 1.855, $p < 0.001$) reflect the importance of body proportions in prostate cancer risk. While not widely studied in the context of prostate cancer, this finding suggests that body composition and its impact on hormonal balance may play a role in disease development (Hsing et al., 2001).
9. **FMH (Family History of Prostate Cancer)**: Family history of prostate cancer, as a risk factor for prostate cancer (OR = 2.312, $p < 0.001$), aligns with studies suggesting shared genetic susceptibility across different malignancies, as well as for prostate cancer itself (Kharazmi et al., 2012). Genetic factors may indeed play a role in multiple cancer types (BRCA1, BRCA2), including prostate cancer.

10. **ALC (Alcohol Consumption)**: The lack of a significant association between alcohol consumption and prostate cancer risk (OR = 0.974, p = 0.871) in this study is in line with some findings (Baumann et al., 2019). The relationship between alcohol and prostate cancer remains a topic of debate.
11. **TBC (Tobacco Use Category)**: The protective effect of tobacco use on prostate cancer risk (OR = 0.331, $p < 0.001$), as indicated in this study, contradicts established evidence linking smoking to increased risk (Huncharek et al., 2010). Further research is needed to understand this discrepancy.

In conclusion, these findings underscore the multifactorial nature of prostate cancer risk. While some factors align with existing literature, such as age and PSA levels, others, like marital status and tobacco use, present intriguing contrasts. These discrepancies highlight the need for continued research to elucidate the complex interplay of genetic, lifestyle, and environmental factors in prostate cancer development.

5.1.4 Determinants of Prostate Cancer Disease Severity Inherent to the Disease at Diagnosis

Disease Characteristics and Indirect Treatment Outcome Measures: Concerning prostate cancer disease characteristics and treatment outcomes, our study provided valuable insights:

1. **Metastasis**: Approximately 30% of the patients had metastatic disease. This aligns with previous studies indicating that metastasis is a significant concern in prostate cancer (Halabi et al., 2016). The presence of metastasis often implies that patients are presenting late, or a with more advanced stage of the disease, requiring aggressive treatment approaches; which may fail at the end of the day. A sub-analysis of the non-metastatic group of patients in our study showed that another 16.81% of the patients had locally advanced disease. The sum of all these is that, up to 46.81% of the patients report to hospital with advanced prostate cancer (made up of locally advanced cancer plus frankly metastatic cancer) which are more difficult to treat. By this, our findings suggest that, in our study, the percentage of patients that present to hospital early for prostae cancer treatment constitutes only 53.19%, compared to about 80% in western countries who have in place, structures and strategies to ensure early diagnosis and cure of prostate cancer (Umberto et al., 2017). This finding is however,

closely in line with what is known already about Ghana, that most of prostate cancer cases (85%) report late to hospital (Globacon 2021), leading to a poor case-fatality rate of about 50% according to the same sources. These are situations that need addressing to stem the tide.

2. **PSA at Diagnosis**: The average PSA level at diagnosis was high (496.391 ng/ml), indicating potentially advanced disease or high risk disease; and an indication of late presentation of the cases. PSA levels are crucial for risk assessment and treatment planning (Thompson et al., 2004). Therefore, this situation may translate into relatively poor treatment outcomes. No wonder our calculated treatment failure rate based on the dynamics of direct and indirect PSA measures (LPSA, and FRM) was a disturbingly high 77.11% (see table 4.3). Generally according to the American Cancer Society (2020), the survival rates for Localized (confined to the prostate) is nearly 100%. For locally advanced disease (spread to nearby structures or lymph nodes, it is also approximately 100%. In contrast, those with distant spread (metastasized to distant organs like bones may have survival rates of around 31%. To attain these, our PSA failure rates must not exceed a peer – reviewed PSA response rate (PSA decline ≥ 50%) to treatment of 68% (Renee Brady-Nicholls et al., 2021). So our attained value of 77.11%, is higher and must be addressed as it may reflect the late presentation of our prostate cases to hospital. On assessing the proportion of the patients that had some response to therapy based on PSA, we invoke the definition that classifies a fifty percent or more, fall of the PSA from the baseline, represents a response to treatment. Based on this, we found that, 45.42% (387 out of 852) FAILED TO RESPOND; ie failed to attain at least a 50% drop in PSA at diagnosis; from the baseline; whilst 54.58% (465 out of 852) did respond, based on the definition. These values reflect the brighter side of our treatment outcomes, that suggests that the SGMC is doing well with its case management; attaining a (PSA-based) response rate of 54.58%; which compares favourably with the expected 68%, according to Renee Brady-Nicholls et al., (2021).

3. **Treatment Modalities**: External beam radiotherapy was the main treatment modality in our study, with additional therapies such as hormonal therapy and chemotherapy. The diversity of treatment

modalities reflects the complexity of managing prostate cancer, with treatment decisions based on disease stage and patient characteristics (Mottet et al., 2017).

4. **PSA Response**: PSA resolution and changes per dose of radiation and treatment modality were observed. PSA response is a key indicator of treatment effectiveness (Mohler et al., 2016). The variability in PSA response underscores the need for individualized treatment plans.
5. **Toxicity**: Treatment toxicity data were available for a subset of patients. Monitoring and managing treatment-related toxicities are essential for maintaining the quality of life in prostate cancer patients (Sanda et al., 2008). Our findings that youger men (p= 0.001), and obese men, (p =0.034) are more succeptible to toxicity than others is expected; and are in line with findings in other studies (Zelefsky et al., 2009, Martin et al., 2018). This new finding should provide our local clinicians with a cue for a high index of suspiscion, so that they keep a close eye on such obese men, or young men, and not be over aggressive with their treatment.

5.1.5 Associations/Correlation Analysis Findings:

Age versus PSA Levels at Diagnosis: In this study, we found a significant association between age and PSA levels at diagnosis ($p = 0.003$, Kruskal-Wallis rank sum test). Older individuals (aged >65) had higher PSA levels. This is in line with numerous international studies. For example, Etzioni et al. (2002) found that PSA levels tend to increase with age in their study conducted in the United States, suggesting age-related changes in the prostate may contribute to higher PSA levels (Etzioni et al., 2002). It may also suggest an increasing disease severity with increasing age.

Ethnicity, Nationality, Marital Status, versus PSA Levels: Our study also revealed associations between ethnicity, nationality, marital status, and PSA levels at diagnosis. For instance, ethnicity ($p = 0.049$) and nationality ($p = 0.030$) exhibited significant associations with PSA levels at diagnosis. These results align with global trends. Hsing et al. (2000) conducted a study in the United States and Asia and observed variations in PSA levels among different ethnic and nationality groups, suggesting genetic and lifestyle factors may influence PSA levels (Hsing et al., 2000).

Age versus ISUP Grade: Our study reports a significant association between age and ISUP grade ($p = 0.009$), with older individuals having a higher median ISUP grade. This finding is consistent with international research. For instance, Albertsen et al. (1998) conducted a study in the United States and found that age is a strong predictor of high-grade prostate cancer, supporting the role of age in the progression of prostate cancer (Albertsen et al., 1998). This suggests that screening to diagnose our patients earlier at a younger age would be beneficial to public health; and indeed, global health.

Ethnicity, Nationality, versus ISUP Grade: Similarly, our findings indicate that ethnicity ($p = 0.049$) and nationality ($p = 0.030$) are associated with ISUP grade, although the associations are not as strong as age. This reflects broader research suggesting that genetic and environmental factors can lead to variations in cancer severity among different demographic groups. For example, studies in Africa by Jemal et al. (2017) have explored the role of genetic diversity in prostate cancer outcomes, underlining the complex interplay of genetics and environment in cancer progression.

Comorbidity versus Adjuvant Treatment: Our study reveals a strong association between comorbidity status and the use of adjuvant treatment ($p = 0.001$). This underscores the importance of considering a patient's overall health. These findings align with international guidelines, such as those from the National Comprehensive Cancer Network (NCCN), which recommend tailoring prostate cancer treatment based on comorbidity status (NCCN, 2020). It also highlights the importance of individualized treatment decisions based on comorbidity status (NCCN, 2020).

Nationality versus Total Treatment Modalities: Our study finds a significant association between nationality and the total number of treatment modalities received ($p = 0.030$). This suggests that treatment approaches may differ among individuals of various nationalities. These variations could be related to cultural factors influencing treatment decisions. International clients may be prone to requesting for or attracting over-aggressive therapy combinations; and this may have to be looked at and checked. This emphasizes the need for addressing disparities in treatment access and decisions based on nationality

(Lichtenberg, 2019). Whether or not this increase in number of treatment modalities potentially led to increased incidence of toxicities in the international clients, was not elucidated by our study.

Age versus Toxicity: Our findings indicate that age is associated with toxicity ($p = 0.001$), with younger individuals experiencing higher toxicity. This aligns with research on treatment-related side effects. Younger patients often receive more aggressive treatments, leading to increased toxicity (Zelefsky et al., 2009). This emphasizes the importance of balancing treatment aggressiveness with age and overall health (Zelefsky et al., 2009).

BMI versus Toxicity: Our study also reports an association between BMI levels and toxicity ($p = 0.034$), with individuals with higher BMI experiencing more toxicity. This is consistent with research indicating that body composition can influence treatment-related side effects; and may be explained by the fact that in obese patients, organ targetting to avoid off-target effects is often difficult and imperfect; and thus prone to side effects/mis-targetting. This suggests that BMI may play a role in treatment-related toxicity in Ghana, similar to findings in other populations (Martin et al., 2018). However, the specific implications of BMI for prostate cancer treatment in Ghana would benefit from further investigation.

5.1.6 Relationship Between Disease Determinants, Disease Severity at Diagnosis (Risk Category) and Treatment Outcomes:

Overall Risk Strata:

1. **'Normal' BMI and Overall High-Risk Localized Prostate Cancer:** Our study found a noteworthy positive relationship between individuals in the 'Normal' BMI group and a higher predilection for overall high-risk localized prostate cancer (OR = 2.34, $p = 0.022$). This suggests that maintaining a 'Normal' BMI may be a risk factor for a more severe form of localized prostate cancer. Interestingly, this finding contrasts with some international studies. For example, a study by Rodriguez et al. (2019) in the United States found that higher BMI was rather associated with an increased risk of aggressive prostate cancer (Rodriguez et al., 2019). So our findings, even though may be unique may need to be researched further with prospective studies for confirmation.

2. **DRE Categories: Ethnicity and DRE Risk Categorization:** We observed that the 'Ewe' (OR = 0.52) and 'GA' (OR = 0.40) ethnicities showed lower-risk level disease based on DRE risk categorization of localised prostate cancer, compared to Akans. This suggests that these ethnic groups may have a reduced predeliction towards being diagnosed with high risk/severe form of localised prostate cancer, based on DRE assessment. While these findings are interesting, they should be interpreted with caution, as other factors may contribute to these associations. Ethnicity's role in prostate cancer risk is a topic of ongoing research, and these findings warrant further investigation.
3. **Low SES and Low-Risk Disease on DRE:** Our study also revealed that 'Low SES' individuals had significantly more low-risk disease, as determined by DRE (OR = 0.58, p = 0.025). This finding suggests that socioeconomic status may somehow, favour low-risk/less severe form of localised prostate cancer. This aligns with a similar recent study conducted in Ghana, i.e. the work by Chinebuah et al. (2020), which highlighted the impact of socioeconomic factors on prostate cancer outcomes in the Ghanaian context (Chinebuah et al., 2020) and found 'low SES' to be favourable. Perhaps more 'low SES' individuals end up not consuming too much of fatty diet, and perhaps, exercise more/ are less sedentary by default). This apparent protection also extends into the next discussion point, about metastasis in the same group.

4. **Metastasis: Low SES and Metastasis:** Low socioeconomic status (SES) was found to be significantly related with a reduced odds of metastasis (OR = 0.67, p = 0.021). This indicates that individuals with lower SES may also have a reduce risk of developing metastatic prostate cancer. These findings contradict global research on the link between socioeconomic disparities and cancer outcomes (Siegel et al., 2017). Studies like the one by Siegel et al. (2017) in the United States have shown that lower SES is linked to a higher risk of advanced stage cancer at diagnosis (Siegel et al., 2017).
5. **Obesity and Metastasis:** Being obese was also significantly related with metastasis (OR = 0.35, p = 0.026), but the odds were reduced (<1), indicating a reduced odds of disease progression in this

group. This finding is intriguing and merits further exploration, as it contradicts international studies. For instance, a study by Cao et al. (2018) in China found that obesity was associated with a higher risk of aggressive prostate cancer (Cao et al., 2018); however it may only confirm the unique nature of prostate cancer disease in Ghana, overall.

6. **Comorbidities and Metastasis:** The presence of comorbidities also yielded a 'reduced odds' link with metastasis (OR = 0.59, p = 0.014). This suggests that having comorbid conditions may be associated with a reduced risk of being diagnosed with a metastastatic prostate cancer. This finding emphasizes the importance of considering a patient's overall health status when assessing prostate cancer risk, as comorbidities may influence disease progression (Schofield et al., 2021). Maybe individuals with one co-morbidity or the other become more self-preserving; and take up a more proactive health-seeking behaviour; the benefit being the increased likelihood of going in for prostate cancer screening regularly, and being diagnosed early in the disease stage.

Toxicity: Marital Status and Toxicity: Single men had higher odds of experiencing toxicity during treatment for prostate cancer (OR = 2.72, p = 0.017). This emphasizes the potential role of social support in coping with treatment-related side effects. Our findings align with research suggesting that marital status can impact cancer treatment outcomes (Boyes et al., 2019, Aizer et al., 2013). These insights may again, emphasize the importance of considering psychosocial factors in prostate cancer managent; and the possible positve roles of theories like the socio-ecological model (McLeroy et al., 1988), and the social cognitive theorey (Bandura, A. 1977, 1986, 1989, 2001, 2006 and 20016), in improving prostate cancer health promotional endeavours.

7. **Family History and Toxicity:** Family history of prostate cancer was observed to be associated with an increased risk of toxicity during treatment (OR = 2.09, p = 0.036). This finding suggests that genetic factors or shared lifestyle habits within families may contribute to increased toxicity risk. While the link between family history and prostate cancer risk is well-established, its association with treatment-related toxicity warrants further investigation (Hjelmborg et al., 2014). Over

aggressive treatment by clinicians knowing that such a client has a family history, may be the reason; meaning that this predeliction to toxicity in this group may be only factitious; but at the same time, patient selection and tailoring of required treatment to clients must be continuously adhered to, by clinicians. They must also assume a high index of suspiscion at all times, to try and avoid these situations.

5.1.7 Predictive Models:

The determinants of prostate cancer metastasis in our study group are BMI, PSA, ISUP, DRE, socio-ecomomic status, activity level of occupation, and marital status. Our model draws some similarities from several studies that have demonstrated a strong correlation between elevated Phi Index values; which predominatly uses PSA and other PSA derivatives or analogues alone to predict the risk of metastasis (Catalona et al., 2011). Phi-index information can be invaluable in tailoring treatment plans for patients with prostate cancer. For those at higher risk of metastasis, more aggressive treatment strategies may be considered to improve long-term outcomes. On the other hand, our model has the advantage of including other demographic and physical variables in the risk estimation; making it more encompasing in its approach. In summary, our study underscores the complex and multifaceted nature of prostate cancer risk assessment in the Ghanaian context. These findings highlight the importance of considering factors such as BMI, socioeconomic status, marital status, and comorbidities when assessing prostate cancer risk. However, some of our results differ from international studies, emphasizing the need for more region-specific and country- specific research to tailor prostate cancer risk assessment and management strategies effectively in Ghana. Further investigations and larger-scale studies are warranted to validate and expand on these finding.

The Prostate Cancer Risk Estimation Model (in reference to table 4.5b)

The multi-parametric prostate cancer risk-estimation model outperforms a PSA alone model in that respect and may be a useful tool similar to the phi- index for prostate cancer risk estimation that exists internationally (Catalona et al, 2011). In our investigation of prostate cancer diagnosis, we scrutinized two distinct diagnostic models: the multiparametric model and the PSA test as a standalone tool.

The multiparametric model showcased impressive results, with a sensitivity of approximately 79.69%, demonstrating its effectiveness in correctly identifying true positives. In tandem, its specificity was commendable, hovering at around 84.57%, indicating its skill in accurately detecting true negatives.

The Positive Predictive Value (PPV) or precision was noteworthy at approximately 84.49%, underscoring the model's precision in categorizing positive instances. Likewise, the Negative Predictive Value (NPV) achieved a substantial value of about 79.82%, confirming the model's prowess in accurate negative predictions.

This comprehensive model delivered an overall accuracy rate of about 82.19%, signifying its proficiency in making correct classifications across both positive and negative classes. The F1-Score, a harmonious blend of precision and recall, was calculated at approximately 82.08%, illustrating a balanced performance.

In addition, the Prevalence, indicating the proportion of positive cases in the dataset, was estimated at around 51.62%, reflecting the prevalence of prostate cancer in our artificially created population. The False Positive Rate (FPR) was found to be approximately 15.43%, shedding light on the model's tendency to incorrectly label negative instances as positive.

The model's performance was further evaluated through various yield metrics. Population Yield, Prevalence Yield, and Sensitivity Yield all provided nuanced insights into its performance across different contexts. Furthermore, an alternative AUC calculation method, approximating 82.13%, further affirmed its diagnostic prowess.

On the other hand, the PSA test as a standalone diagnostic tool demonstrated respectable sensitivity of about 65.96% and noteworthy specificity of around 80.00%. Its Positive Predictive Value (PPV) reached approximately 77.61%, emphasizing its precision in classifying positive cases, while the Negative Predictive Value (NPV) stood at about 69.05%, indicating precision in negative classifications.

Overall accuracy was estimated at around 72.24%, and the F1-Score, an indicator of balanced performance, measured approximately 71.71%. In the context of the population prevalence of prostate cancer, which was

43.56%, the PSA test yielded a Population Yield of about 28.79%. Prevalence Yield matched sensitivity at 65.96%.

Lastly, an AUC of approximately 72.98% was obtained through an alternative calculation method.

In conclusion, both models exhibit strengths in diagnosing prostate cancer. The multiparametric model excells in terms of sensitivity, specificity, and overall accuracy, making it a robust choice for precise classification. In contrast, the PSA test, while demonstrating respectable performance, may benefit from complementary diagnostics to enhance its accuracy. The choice between these models should consider the specific diagnostic needs and resources available, as each model offers unique advantages and trade-offs in the pursuit of accurate prostate cancer diagnosis. This multiparametric prostate cancer case-detection/risk estimating model bears some potential for future screening endeavours. It has to be trained, tested, re-tested and validated on real or simulated populations which have a prostate cancer prevalance akin to that of the Ghanian community, which stands at about 7%; (Wiredu et al, 2006), to make it more reliable.

Selection of Diagnostic Thresholds for the Models:

A discussion on how we intend to select the diagnostic thresholds for the models can be found, at the appendix 5 of this thesis.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

1. **Increasing Trend in Prostate Cancer Visits:** There is an increasing burden of prostate cancer cases in Ghana, evidenced by the noticeable upward trend in patient visits to the Sweden Ghana Medical Center (which is one of the leading cancer treatment centers in Ghana), for prostate cancer care, especially in recent years (2018-2023).
2. **Late Presentation/a predominance of late presentation cases:** most prostate cancer cases in Ghana present rather late. Up to 46.19% (ie almost 50%) of all the cases present late (either as locally advanced or frankly metastatic prostate cancer; meaning that steps need to be taken at all fronts to stem the tide to ensure that we start diagnosing more early stage diseases that are ammenable to cure. In addition the late presentations often go with poor treatment outcomes, and that was evident in our finding that, on the surface, about 77% of the patients don't do well, (in absolute cure terms); when we consider treatment outcomes from sustained PSA response dynamics: (even though initial response rate was 54.58%). This further confirms the need for early detection of prostate cancer cases in Ghana, as a way of improving treatment outcomes in the long run.
3. **Ethnic Disparities:** Ethnicity plays a significant role in prostate cancer case proportions and disease characteristics in Ghana, with statistically significant differences observed among ethnic groups.
4. **Marital status, occupation, family history, alcohol use**: This study highlights the significance of marital status, occupation, socio-economic status, and genetics in prostate cancer risk and outcomes. Additionally, it calls for attention to alcohol consumption as a potential health promotion area.
5. **Comorbidities:** The frequency of comorbidities amongst prostate cancer patients is low; with hypertension and diabetes being the predominant comorbid condition amongst the study group. Individuals with comorbidities were more likely to need adjuvant therapy, even though they get diagnosed mostly with non-metastatic prostate cancer.
6. **Disease Determinants:** The various determinants of prostate cancer include; sex; maleness, 100%(all our patients in the study group, were males); age 55 and above (75%); modal age, 65 to

74(44.6%); ethnicity; (Akan; 55.52%, Ewe, 14.91%); BMI above 24.5Kg/m^2 (79.48%); but overweight alone is (59.3%): married; (70%); high socio-economic status,(59.3%); sedentary occupation, (42.9%) professionals' occupational group (40.38%; but also retirees, 21.60%); urban living (74.79%), and (PSA) a median PSA of 29ng/ml and above; explaining more than fifty percent of the cases; and a PSA of 12.9 ng/ml and above, explaining 75% of the cases ie (the 75^{th}. Percentile).

A prostate cancer detection/risk estimation model obtained from combining PSA and various determinants of prostate cancer disease is given by, Logit DIAG = -0.0199958 + 0.0865589 * LIN_CD - 0.0634608 * BMI_CD + 0.1187077 * AGE_CD + 0.0847289 * MAR_CD - 0.034675 * ETH_CD + 0.1870673 * SES - 0.1870553 * ACT + 0.1194774 * FMH - 0.195909 * TBC + 0.0000351 * PSA…(equation, S1). And it outperformed a PSA alone model considerably. This is a potential prostate cancer screening tool; which if developed, could contribute immensely to improving the efficiency of prostate cancer screening initiatives in Ghana.

7. The determinants of prostate cancer metastasis in our study group are BMI, PSA, ISUP, DRE, socio-ecomomic status, activity level of occupation, and marital status.

From our study, the risk/probability of metastasis in prostate cancer (between 0 and 1) is predicted by the mathematical model (Note that, where **LOGIT (X) means, log((P(X =1)/(1−P(X=1), all the ensueing equations hold):-**

Log(odds of MET_CD) = -13.496 + (0.004 * AGE) - (0.109 * AGE_CD) - (0.068 * MAR_CD) + (0.074 * ETH_CD) - (0.688 * SES) + (0.873 * ACT) - (0.945 * BMI_CD) + (0.097 * LINWH) - (0.313 * LIN_CD) - (0.019 * PND) + (0.472 * PND_CD) - (0.315 * FMH) + (0.397 * ALC) - (1.137 * TBC) + (0.199 * LOC_CD) + (3.946 * DRE_CD) + (0.002 * PSA) + (0.390 * ISUP) …….(1)

This equation/mathematical model has a Sensitivity of 85.651%; Specificity of 95.45%; Positive Predictive Value of 90.84%; Negative Predictive Value of 92.65% and an accuracy of 75.31%. The "log likelihood" of (-76. 516265), psuedo R^2 of 70.53%. The likelihood ratio chi-squared test (LR chi2=366.22)

was highly significant ($p < 0.05$), indicating the model's statistical significance. AUC of ROC curve = **90.55%;** $YIELD_p$= **68.71% and** $YIELD_s$= **95.45%. This could be a viable tool that would help improve equity and accessibility to prostate healthcare, and contribute to quicker detection of metastasis in prostate cancer in Ghana.**

8. The determinants of treatment response in prostate cancer in our study group are BMI, PSA, ISUP, DRE, the presence or absence of metastasis at diagnosis, activity level of occupation, and marital status.
    a. Treatment response in prostate cancer terms of PSA Resolution is predicted by the equation:

Mvreg (RPSA) = 15.57919 + 2.724728 * DRE_CD + 0.9613279 * PSA – 14.60611 * ISUP – 9.409311 * MET_CD + 71.84873 * ACT – 17.68221 * BMI ……..(2)

This model predicts the percentage/fractional change in RPSA, given certain parameters.

a. Treatment response in prostate cancer in terms of PSA Resolution per Number of Treatment Modalities adminsitered is predicted by the mathematical equation:

Mvreg (PSATM) = -2.079948 + 0.9141269 * PSA – 13.70087 * BMI – 21.08416 * ISUP – 22.17412 * DRE_CD – 10.94641 * MET_CD + 37.86609 * ACT – 2.006442 * AGE_CD …..(3)

This model predicts the percentage/fractional change in PSATM, given certain parameters.

9. From 6, 7 and 8, it is implied that BMI, and the other disease determinats, could help improve the predictive value of PSA in detecting prostate cancer in individuals, by risk estimation/risk calculation, determining the presence of metastasis in prostate cancer; (as well as predicting the nature of treatment response in treating prostate cancer disease) based on our data from the SGMC.
10. Single men, younger patients, patients with a family history of prostate cancer and patients with co-morbidities are identified as vulnerable groups for the development of toxicity in prostate cancer treatment.
11. Patients with comorbidities and international patients have a predeliction to attracting multiple treatment modalities/additional adjuvant therapy in prostate cancer treatment.

6.2 RECOMMENDATIONS:

6.2.1 Recommendations to Health Systems' Authorities:-

1. **Increase Awareness and Education**: There is the need for NGOs and Academics to collaborate with the Ghana Ministry of Health and non-governmental organizations to raise awareness about prostate cancer, with a specific focus on high-risk ethnic groups like Akans, Ga, and Northern Ghanaian men; through nationwide campaigns and educational programs.
2. **Enhance Early Detection Programs**: The Ghana Health Service is encouraged to strengthen and expand early detection programs for prostate cancer, including regular screenings, especially for men over 45, in urban and periurban areas. This would enhance early detection and cure of prostate cancer and help stem the usual tide of late presentation of cases to the hospital with its attendant poor treatment outcomes.
3. **Ethnic-Specific Interventions**: There is the need for the ministry of health to develop targeted interventions and policies, for high-risk ethnic groups, such as the Akans, in collaboration with local healthcare providers and community leaders to address prostate cancer disparities effectively.
4. The ministry of health and the Ghana Health service should take measures to promote a healthy lifestyle through public health campaigns targeting urban areas, emphasizing BMI control; and implement workplace wellness programs, particularly for sedentary job sectors, to encourage physical activity. Establish genetic counseling services within Ghana Health Service facilities to support individuals with a family history of prostate cancer. Strengthen anti-alcohol initiatives and campaigns across both urban and rural areas in collaboration with the Ministry of Health.
5. **Comprehensive Cancer Registry**: The Ghana Health Service needs to lead the estalishment of a National Cancer Registry; With which relevant bodies, like universities, colleges, and cancer hospital and research centers would collaborate to enhance data collection and analysis, ensuring that trends in prostate cancer and other malignancies are continuously monitored to inform healthcare policies.

6. **User friendly electronic applications Apps**: The mathematical models identified in this study may be developed into user-friendly nomograms/mobile applications to aid healthcare improvements going forward.

6.2.2 Recommendations to Sweden Ghana Medical Center's Authorities

Monitoring Patients at Increased Risk of Treatment Toxicity:

1. **Single Men (Marital Status)**: They are encouraged to implement a specialized monitoring program for single men undergoing prostate cancer treatment, to forestall treatment toxicity. Single individuals have been identified as having a higher risk of treatment toxicity. This will help them to regularly assess their treatment response and side effects, ensuring timely intervention if toxicity occurs.
2. **Patients with a Family History of Prostate Cancer**: They are encouraged to create a dedicated surveillance plan for patients with a positive family history of prostate cancer. Due to their increased risk of toxicity, they should consider closely monitoring their treatment progress and any potential side effects. It would also be good to offer them genetic counseling to assess hereditary factors that may influence treatment response.
3. **Younger Patients (Age)**: Recognize that younger patients may be more vulnerable to treatment toxicity. Develop age-specific treatment guidelines and monitoring protocols to ensure their safety and minimize side effects. Regularly assess their functional status and adjust treatment plans accordingly.
4. **Patients with Comorbidities**: Identify patients with comorbid conditions, especially hypertension and diabetes, which have been associated with an increased need for adjuvant therapy, and risk of toxicity. Collaborate with specialists to manage comorbidities effectively during prostate cancer treatment, reducing the likelihood of treatment-related complications.
5. **International Patients Accessing care at SGMC:** These patients for some reason were found to have a predeliction to receiveing a high number of treatment modalities. The effect of this on toxicity

risk is however yet to be deciphered. This situatuon should be closely looked at, to make sure it does not become counter-productive to the quality of care.

6. The SGMC authorities are encouraged to Implement regular symptom monitoring and patient education to detect and address treatment toxicity promptly. Embrace a multidisciplinary care approach involving oncologists, urologists, nurses, and specialists. Provide psychosocial support to help patients cope with treatment-related challenges. Promote data collection, research, and cancer prevention efforts for sustainable cancer care at SGMC.
7. Finally, the SGMC authorities are encouraged to implement some degree of expansion in terms of their bouquet of services, (to include a cancer prevention and early detection unit) to conduct health education, health promotion (to prevent prostate cancer) and screening for early diagnosis of prostate cancer as a more proactive way of ensuring that the outcomes of treatment of their prostate cancer patients improve in the long run. By this they can identified corporate bodies, liaise with them and conduct cordinated, and sustained workplace cancer prevention and screening activities for their employees; as the economically more efficient approach to preventing, and/or improving prostate cancer outcomes, as a whole, in Ghana.

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APPENDIX 1

Dissemination Of Results

Results shall be disseminated through organized presentations to the Ensign Global College Faculty, the management of the study site and presentation to policy makers to help them shape public policy; these shall be done by the research team. Manuscripts would be generated for submission to peer – reviewed journals so that the knowledge and experience may be shared. This would be done jointly by the management of the study sites and the research team.

APPENDIX 2

The Details of Prostate Cancer Management, Toxicity and Iatrogensis:

TNM Staging of Prostate Cancer and Categorization into Localized, Locally Advanced, and Metastatic Disease:

Prostate cancer is staged using the TNM system, which evaluates the extent of the tumor (T), involvement of regional lymph nodes (N), and presence of distant metastases (M). Additionally, sub-staging (a, b, c) provides more specific information within each primary stage. Here are the full details of the TNM staging for prostate cancer (National Comprehensive Cancer Network, 2021).

1. T Staging:

- TX: Primary tumor cannot be assessed.
- T0: No evidence of primary tumor.
- T1a: Incidental tumor found in less than 5% of resected tissue.
- T1b: Incidental tumor found in more than 5% of resected tissue.
- T1c: Tumor identified via needle biopsy due to elevated PSA but not palpable during DRE.
- T2a: Tumor involves one-half or less of one lobe.
- T2b: Tumor involves more than one-half of one lobe but not both lobes.
- T2c: Tumor involves both lobes.
- T3a: Tumor extends through the prostate capsule.
- T3b: Tumor invades the seminal vesicles.
- T4: Tumor invades adjacent structures, such as the bladder or rectum.

2. N Staging:

- NX: Regional lymph nodes cannot be assessed.
- N0: No regional lymph node involvement.
- N1: Regional lymph node metastasis present.

3. M Staging:

- MX: Distant metastasis cannot be assessed.
- M0: No distant metastasis.
- M1a: Distant metastasis to non-regional lymph nodes.
- M1b: Distant metastasis to bones.
- M1c: Distant metastasis to other organs.

Categorization into Localized, Locally Advanced, and Metastatic Disease:

- Localized Disease: Prostate cancer that is limited to the prostate gland (T1-T2) without regional lymph node or distant metastasis (N0, M0).

- Locally Advanced Disease: Prostate cancer that extends beyond the prostate capsule (T3) or invades adjacent structures (T4) without distant metastasis (M0).
- Lymph node spread; N0 (no spread); or N1 lymph nodal spread present.
- Metastatic Disease: Prostate cancer that has spread to non-regional lymph nodes (M1a) or distant sites, such as bones (M1b) or other organs (liver, lungs, kidneys, or very rarely, the testes) (M1c) (Kyei et al., 2012).

Note: for localised disease, the TNM staging may further be combined into prognostic risk groups (low, intermediate, high). This is done based on additional factors like PSA levels, Gleason score, and clinical stage on DRE, to guide treatment decisions and predict outcomes.

Also, while DRE provides valuable information, it has limitations in detecting small or early-stage tumors and assessing the tumor's precise location and size. Therefore, additional imaging and biopsy are essential for accurate staging and treatment planning.

Even though localised prostate cancer is associated with better prognosis, it is by no means a homogenous disease, so it is stratified based on PSA, DRE and ISUP as follows:-

2.10 PSA Stratification of Prostate Cancer Disease:

Prostate-specific antigen (PSA) is a biomarker commonly used to screen for and monitor prostate cancer. PSA levels in the blood are measured, and based on the values obtained, the cancer is stratified into different risk categories (for localised disease only):

- Low-Risk Prostate Cancer: PSA < 10 ng/mL
- Intermediate-Risk Prostate Cancer: PSA 10-20 ng/mL
- High-Risk Prostate Cancer: PSA > 20 ng/mL (National Comprehensive Cancer Network, 2021).

While PSA stratification provides valuable information on the tumor's aggressiveness and prognosis, it is essential to consider additional factors, such as Gleason score/ISUP grade, clinical stage and imaging results, for comprehensive risk assessment and treatment decision-making.

2.11 Prostate Cancer Histological Grades: also called the Gleason Score/ISUP Grade

Gleason Score:

The Gleason scoring system is a critical component of prostate cancer pathology reporting. It assesses the architectural patterns of tumor cells observed in prostate biopsies or resected specimens. The pathologist assigns one primary Gleason grade (ranging from 1 to 5) to the most prevalent tumor patterns/architecture observed in the biopsy; and another secondary Gleason grade (ranging from 1 to 5) for the second most predominant pattern/architecture observed on the biopsy. The sum of these two grades yields the Gleason score (also called the Gleason sum score in alternative parlance), ranging from 2 to 10. A higher Gleason score indicates a more aggressive tumor with a worse prognosis (Epstein et al., 2016).

For instance, a Gleason score of 3 + 3 = 6 indicates a well-differentiated tumor with a low-grade pattern, while a Gleason score of 4 + 3 = 7 suggests a tumor with a primary pattern of moderately differentiated cells and a secondary pattern of poorly differentiated cells (Epstein et al., 2016).

The International Society of Urological Pathology (ISUP) Grade:

In recent years, the ISUP has introduced a new grading system that simplifies prostate cancer grading by classifying tumors into five grades based on their histological patterns. This system aims to provide more prognostic accuracy and reduce interobserver variability compared to the traditional Gleason scoring.

The ISUP grading system categorizes tumors as follows:

- ISUP Grade 1: Tumors with only well-formed glandular patterns Gleason score ≤ 6).
- ISUP Grade 2: Tumors with a predominance of glandular patterns but with some poorly formed glands [Gleason score of 7 (3 + 4)].

- ISUP Grade 3: Tumors with a predominant, but not exclusive, poorly formed glandular pattern [Gleason score 7 (4 + 3)].
- ISUP Grade 4: Tumors with a predominant, poorly formed glandular pattern or cords, or single cells [Gleason score = 8(4+4)].
- ISUP Grade 5: Tumors with a predominantly non-glandular pattern [Gleason score ≥ 8 (ie 4+5, 5+4, or 5+5)] (Epstein et al., 2016).

  So the risk strata or categories based on ISUP grade/Gleason score is as follows:

  ISUP 1; given that it is localised disease = Low-Risk

  ISUP 2 and 3; given that it is localised disease = Intermediate-Risk

  ISUP 4 and 5; given that it is localised disease = High-Risk.

2.12 Overall Risk Stratification of Prostate Cancer for Treatment (D'Amico Classification):

According to the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines,

The overall risk strata for **localised prostate cancer** can be obtained as follows: -

The overall risk stratification of prostate cancer for treatment is determined based on the combination of three risk parameters: PSA, DRE, and ISUP risk groups (Mohler et al., 2020).

1. If all three risk parameters (PSA, DRE, and ISUP) yielded 'low risk' for a subject, the patient is categorized as 'overall low risk' for prostate cancer. Usually, a single modality is enough for treatiing such prostate cancer.
2. On the other hand, if any one of the three risk parameters (PSA, DRE, or ISUP) yielded a 'high risk' category for a subject, the patient iss assigned an 'overall high risk' for prostate cancer. Usually, multi-modal therapies are combined to treat such prostate cancer.
3. In cases where all three risk parameters were categorized as 'intermediate risk,' or two risk parameters were 'intermediate risk' in the presence of one 'low risk' parameter, or one risk parameter was 'intermediate risk' in the presence of two 'low risk' categories, the patient is classified under the 'overall intermediate risk' category for prostate cancer treatment (Mohler et al., 2020). Usually, bimodal mix of therapies may suffice for treatment of such prostate cancer.

Combining PSA stratification, Gleason scores/ISUP grade, and disease staging by DRE allows for a multi-dimensional approach to risk stratification, facilitating more precise treatment planning and improved patient outcomes.

Conclusion:

Prostate cancer risk stratification using a combination of PSA, Gleason scores/ISUP grade, and disease staging by DRE plays a crucial role in guiding treatment decisions. A comprehensive assessment of these factors helps differentiate patients into low, intermediate, and high-risk categories, enabling personalized treatment plans and optimal management of the disease.

Summarised staging of prostate cancer for treatment decisions:

Prostate cancer disease may also be categorised as localised disease, locally advanced disease, oligometastatic disease (usually, a diagnosis in retrospect), or metastatic disease. This profiling allows tailored treatment.

2.13 Treatment of Prostate Cancer using Various Modalities; and Treatment Outcome Measurements:

Introduction:

The treatment of prostate cancer depends on several factors, including the stage of the disease (localised disease, locally advanced disease, or metastatic disease), the disease risk stratification obtained from the above discussions; the patient's age and overall health(eg, presence of comorbidities), and their preferences. Various treatment modalities are available, and each aims to achieve optimal outcomes while minimizing side effects. The main expected outcomes of the various modalites of disease include cure, clinical failure/local/distant-recurrence/treatment failure, biochemical recurrence, hormone refractoriness, or disease progression. The measurement and monitoring of treatment outcomes is essential to assess the effectiveness of each modality and improve patient care. The various treatment modalities include the following (Akpinar et al., 2017; Alexander et al. 2010):-

1. Active Surveillance: Active surveillance is suitable for low-risk prostate cancer with a Gleason score of 6 or lower and a PSA level below 10 ng/mL. It entails actively following-up the suitable patient every six months at the clinic, during which a detailed history is taken, DRE done, and PSA repeated every 6 months, and biopsy done once the History and Physical Examination, DRE/PSA (or a necessary multi-parametric MRI) show any signs of disease progression (eg an abnormal PSA rise during follow-up in active surveillance). This makes sure that any disease progression can be quickly picked up and treated for cure. The treatment intention here is cure.

- Outcomes are measured through regular PSA tests, DRE, and periodic/tailored prostate biopsies to monitor disease progression. Any progression to higher-risk disease triggers the initiation of active treatment.

2. Surgery (Radical Prostatectomy): Radical prostatectomy involves the surgical removal of the entire prostate gland and surrounding tissues. It is indicated for localised disease.

- Outcome measurement includes assessing surgical success (complete removal of the tumor), post-operative complications, the extent of achievement of the trifecta effect, and the need for additional treatments (Kyei, and Mensah et al., 2023).
- Functional outcomes are also evaluated, such as urinary continence and erectile function recovery (the trifecta effect; Kyei, and Mensah et al., 2023).

3. Radiation Therapy:

a. External Beam Radiation Therapy (EBRT):

- EBRT delivers high-energy rays externally to target and destroy cancer cells.
- Outcome measurement includes PSA response, tumor shrinkage on imaging, and assessment of radiation-related side effects.

b. Brachytherapy:

- Brachytherapy involves placing radioactive sources directly into the prostate gland to deliver targeted radiation.
- Outcome measurement includes PSA response, tumor control rates, and evaluation of urinary and rectal side effects.

4. Androgen Deprivation Therapy (ADT): ADT aims to reduce androgen (testosterone) levels to inhibit prostate cancer growth.

- Outcome measurement involves monitoring PSA levels and assessing the response to hormonal therapy. It is used primarily for metastatic disease.
- Long-term side effects, including osteoporosis and cardiovascular risks, are also evaluated.

5. Chemotherapy: Chemotherapy may be used for advanced or metastatic prostate cancer.

- Outcome measurement includes PSA response, tumor size reduction, and evaluation of overall survival and quality of life.

6. Targeted Therapy: Targeted therapies, such as Abiraterone and Enzalutamide, are used in advanced prostate cancer cases.

- Outcome measurement includes PSA response, disease progression, and assessment of treatment-related adverse events.
- Immunotherapy: Immunotherapies like Sipuleucel-T boost the immune system to target cancer cells.

7. Outcome measurement involves monitoring PSA levels, assessing overall survival, and evaluating treatment-related immune responses.
8. Monomodal, bimodal, trimodal and multimodal therapies: based on disease aggressiveness and severity as determined by the grade and stage, any number of the above modalities of treatment may be combined variously to provide the most comprehensively effective; but tailored therapy for the index patient. Steps are taken to limit toxicity or iatrogensis in all of these processes.

Conclusion:

The treatment of prostate cancer involves a range of modalities tailored to each patient's unique situation. Measuring treatment outcomes is crucial for assessing treatment effectiveness, guiding treatment decisions, and optimizing patient care. Outcome assessment should encompass PSA response, tumor control rates, functional outcomes, side effect profiles, and overall survival to ensure the highest standards of care for prostate cancer patients.

2.14 Iatrogenesis and Toxicity/Side Effects of Prostate Cancer Treatment Modalities:

Introduction:

Prostate cancer treatment modalities aim to eradicate or control cancer cells. However, some treatments may inadvertently cause iatrogenic harm or lead to toxicities and side effects. Understanding and managing these adverse effects are crucial for delivering high-quality care and improving patient outcomes.

1. Surgery (Radical Prostatectomy): Iatrogenesis: Potential complications of radical prostatectomy include surgical site infections, urinary incontinence, and erectile dysfunction (Akpinar et al., 2017).

- Toxicity/Side Effects: Post-operative complications may include urinary leakage, urinary retention, and bowel dysfunction. Erectile dysfunction can also occur due to nerve damage during surgery (Sathianathen et al., 2018).

2. Radiation Therapy: Iatrogenesis: Radiation therapy may lead to secondary malignancies in the long term, though the risk is relatively low (Berrington de González et al., 2016).

- Toxicity/Side Effects: Acute side effects of radiation therapy include fatigue, skin irritation, and diarrheoa. Long-term effects may involve urinary problems, bowel changes, and sexual dysfunction (Mottet et al., 2017).

3. Androgen Deprivation Therapy (ADT): Iatrogenesis: ADT can lead to osteoporosis and increased risk of fractures (Hamilton et al., 2016).

- Toxicity/Side Effects: ADT may cause hot flashes, decreased libido, erectile dysfunction, and mood changes. It can also lead to metabolic syndrome, weight gain, and insulin resistance (Shahinian et al., 2005).

4. Chemotherapy: Iatrogenesis: Chemotherapy can cause myelosuppression, leading to decreased blood cell counts (Freedman et al., 2016).

- Toxicity/Side Effects: Common side effects include nausea, fatigue, hair loss, and increased susceptibility to infections. Chemotherapy can also lead to peripheral neuropathy and anemia (Basch et al., 2014).

5. Targeted Therapy: Iatrogenesis: Targeted therapies can lead to off-target effects on normal cells.

- Toxicity/Side Effects: Adverse effects may include hypertension, liver toxicity, fatigue, and gastrointestinal disturbances (Basch et al., 2012).

6. Immunotherapy: Iatrogenesis: Immunotherapies may lead to autoimmune reactions.

- Toxicity/Side Effects: Common side effects include fatigue, flu-like symptoms, and skin rashes. Severe immune-related adverse events affecting various organs can also occur (Michot et al., 2016).

Conclusion:

Prostate cancer treatment modalities are associated with various iatrogenic and toxic effects, which can impact patients' quality of life and overall well-being. Adhering to the highest standards in healthcare requires close monitoring of patients during treatment, early detection and management of adverse effects, and comprehensive patient education to ensure informed decision-making.

APPENDIX 3

A Note on how Missing Values were Handled during Data Processing

1. Age Missing: For patients with missing age values, it was best to remove their entire records from the dataset, as accurate age information was crucial for analysis and interpretation.
2. Continuous Variables (Weight, Height, BMI, PSA Variables): For continuous variables with missing values, such as weight, height, BMI, and most PSA variables (except 'Fail PSA'), a reasonable approach was to use the nearest-neighbor rule for imputation. The team calculated the average of the values of the nearest neighbors in terms of other relevant variables (e.g., age, gender) and used that as the imputed value.
3. Fail PSA: If 'Fail PSA' had missing values and the information was not provided, it was appropriate to leave them as truly missing values, as these missing values might not have been imputable accurately.
4. Grays of Radiation Treatment: In case there were missing values for 'Grays of Radiation Treatment Given,' the team replaced these with '1 Gray' as a conservative approach when exact information was not available.
5. Adjuvant and Additional Treatment Modalities: For missing values in the adjuvant treatment or other additional treatment modalities, it was reasonable to assume that no additional treatment was given. In the treatment modalities column, a new category 'Zero Treatment Modalities' was created to represent these cases.
6. Gold Seeds Treatment: For 'Gold Seeds' treatment, which was equal to zero treatment, the team recorded them as 'Zero Treatment Modalities' as well, considering that no actual additional treatment was administered.
7. Number of Treatment Given Divisor: To compute the 'Number of Treatment Given Divisor,' which was used as the numerator for the PSA resolution per the number of treatment given, the team calculated it as (1 + the total number of treatment modalities given) and recorded it under its respective column.
8. Categorical Data: If categorical data was missing, it was reasonable to leave it as missing. Trying to impute categorical values could introduce bias and misrepresentation.
9. ISUP and Gleason: For ISUP and Gleason scores, even though they were represented numerically, they were not parametric and should not have been interpolated. If missing, they were left as missing, and the team worked with the available data.
10. Metastasis: For missing values under metastasis, they were replaced with 'No Metastasis' or coded as '0,' assuming no evidence of metastasis.
11. Domain knowledge was utilized for imputation where necessary.

By following these guidelines, the team maintained data integrity while handling missing values in the dataset. Transparency in the data processing and imputation methods was considered essential for the validity of the analysis.

APPENDIX 4

Supplementary charts, tables and graphs:

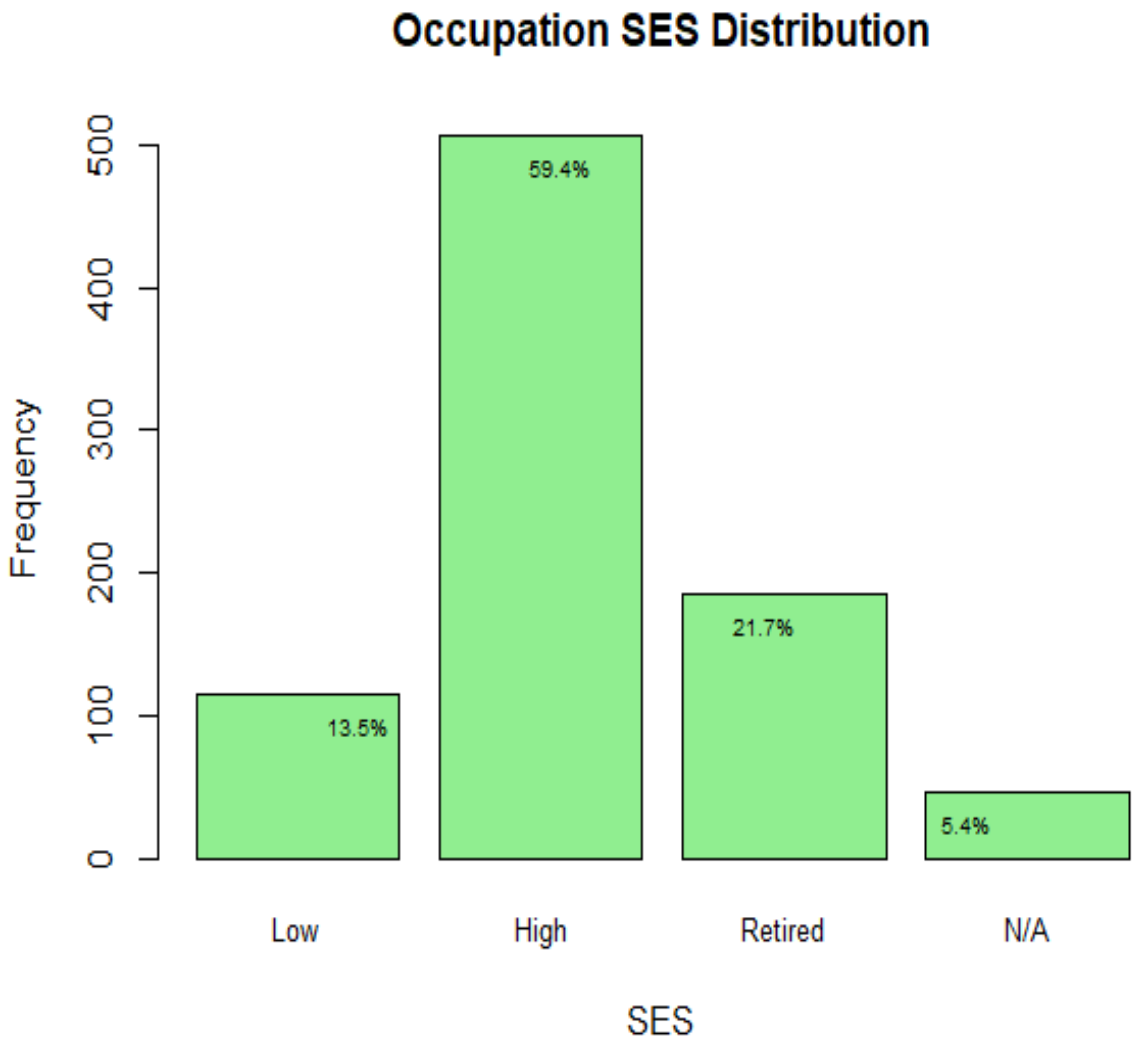

FIG 4.6 SOCIO-ECONOMIC STATUS BY OCCUPATION

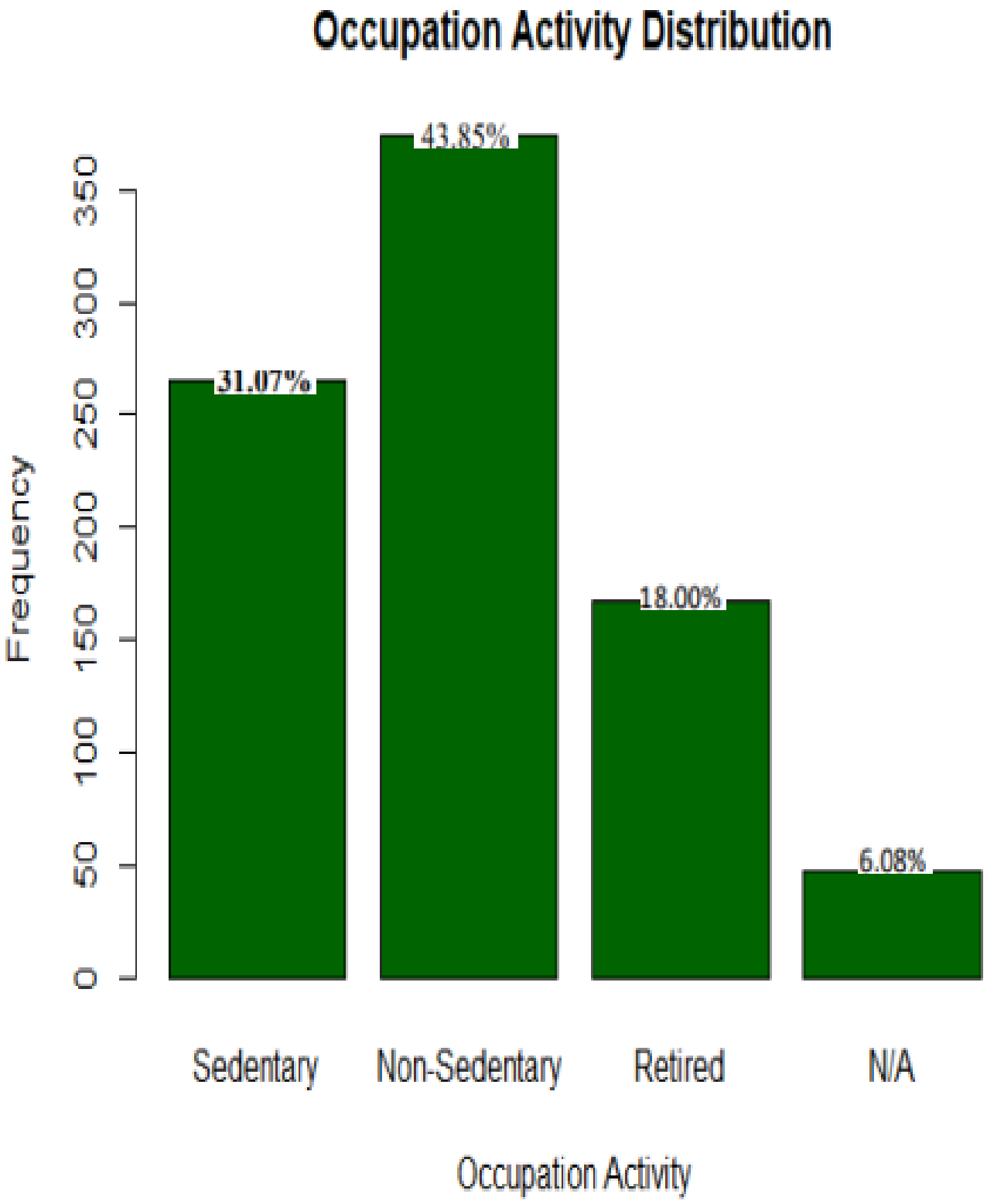

FIG 4.7 ACTIVITY LEVEL BY OCCUPATION

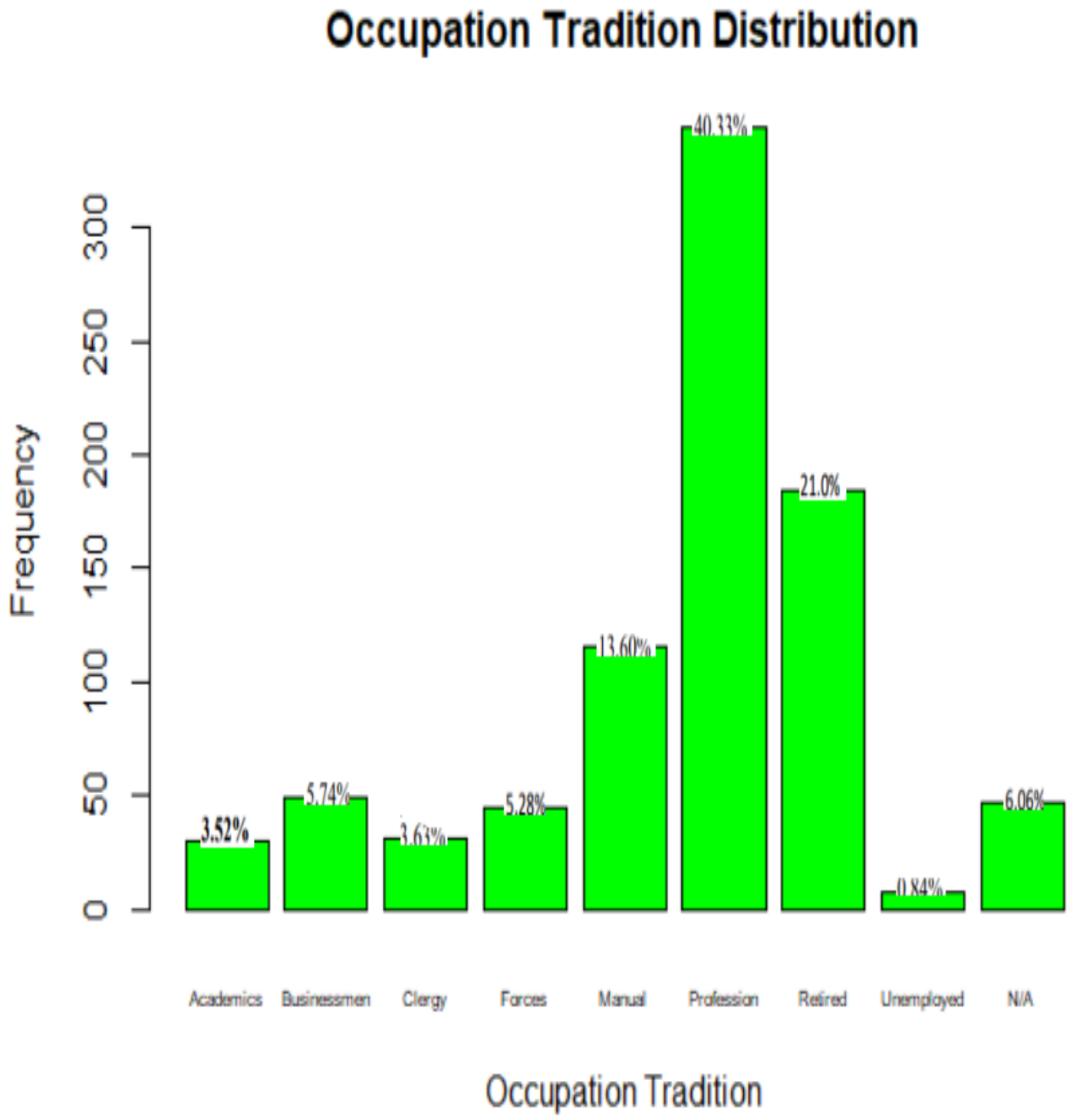

FIG 4.8 TRADITIONAL OCCUPATIONAL GROUPINGS

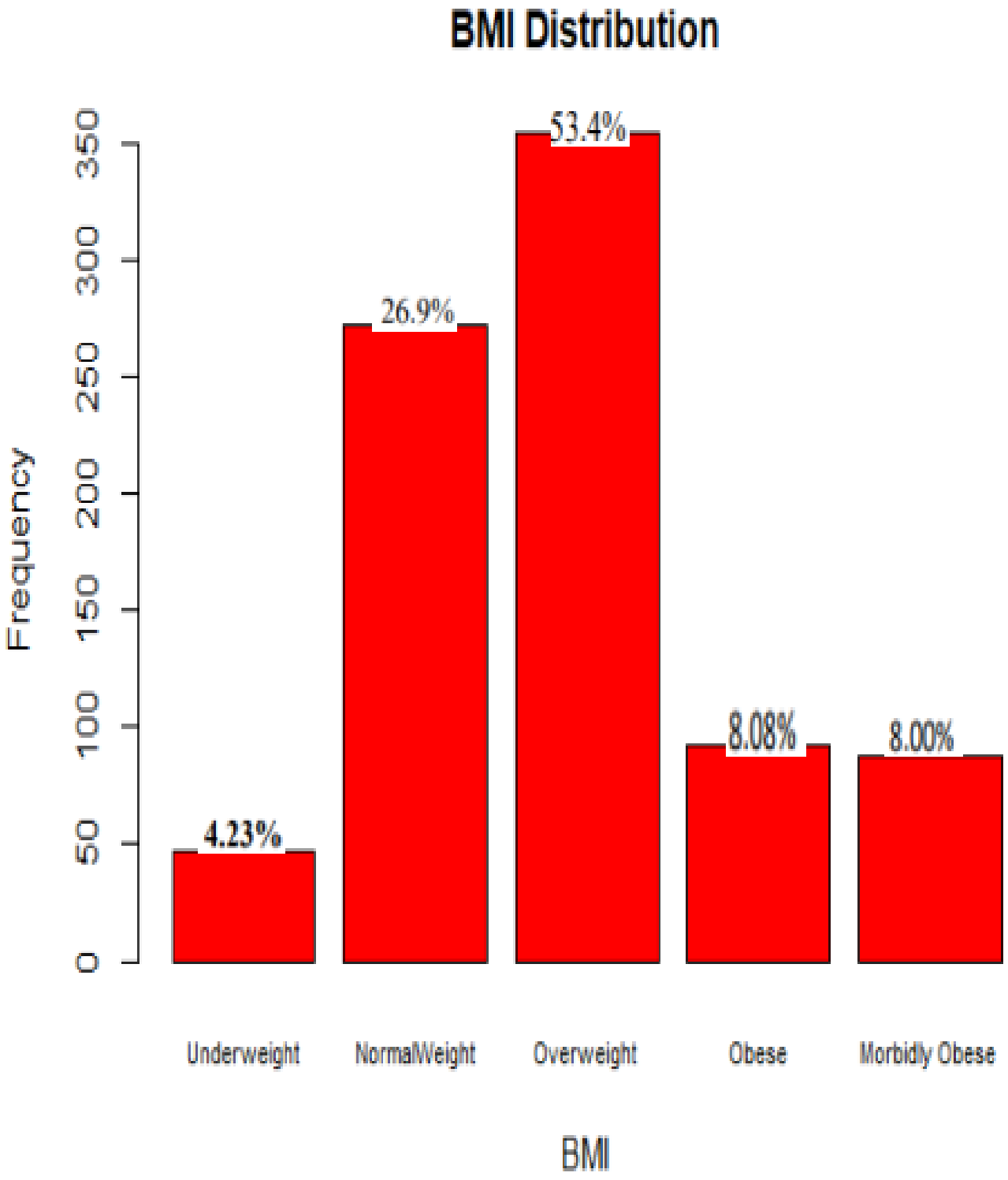

FIG 4.10 BMI DISTRIBUTION

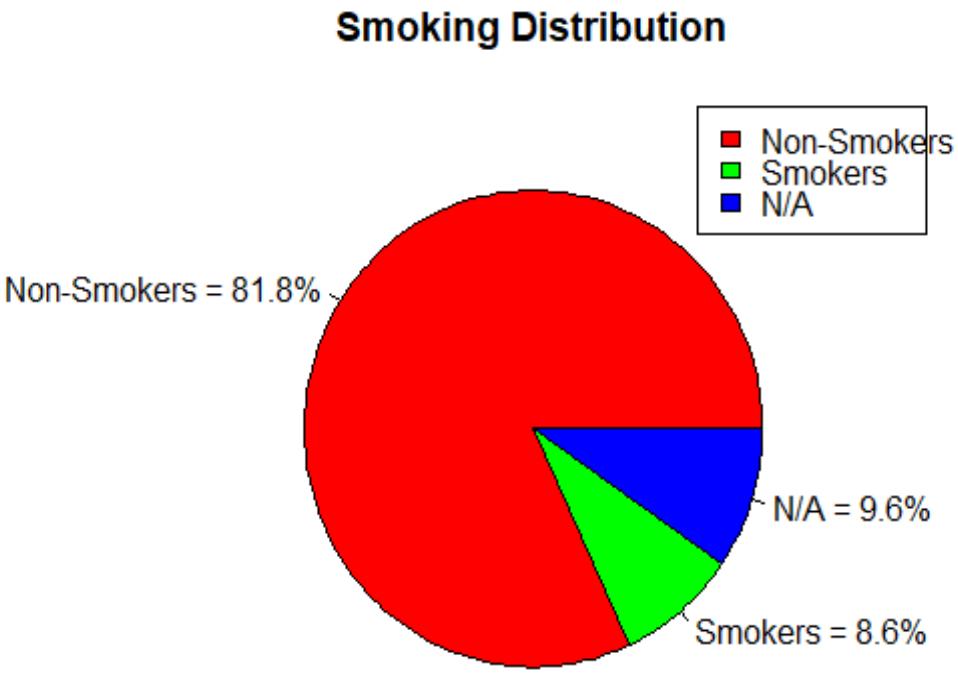

FIG 4.11 SMOKING AMONGST STUDY PARTICIPANTS

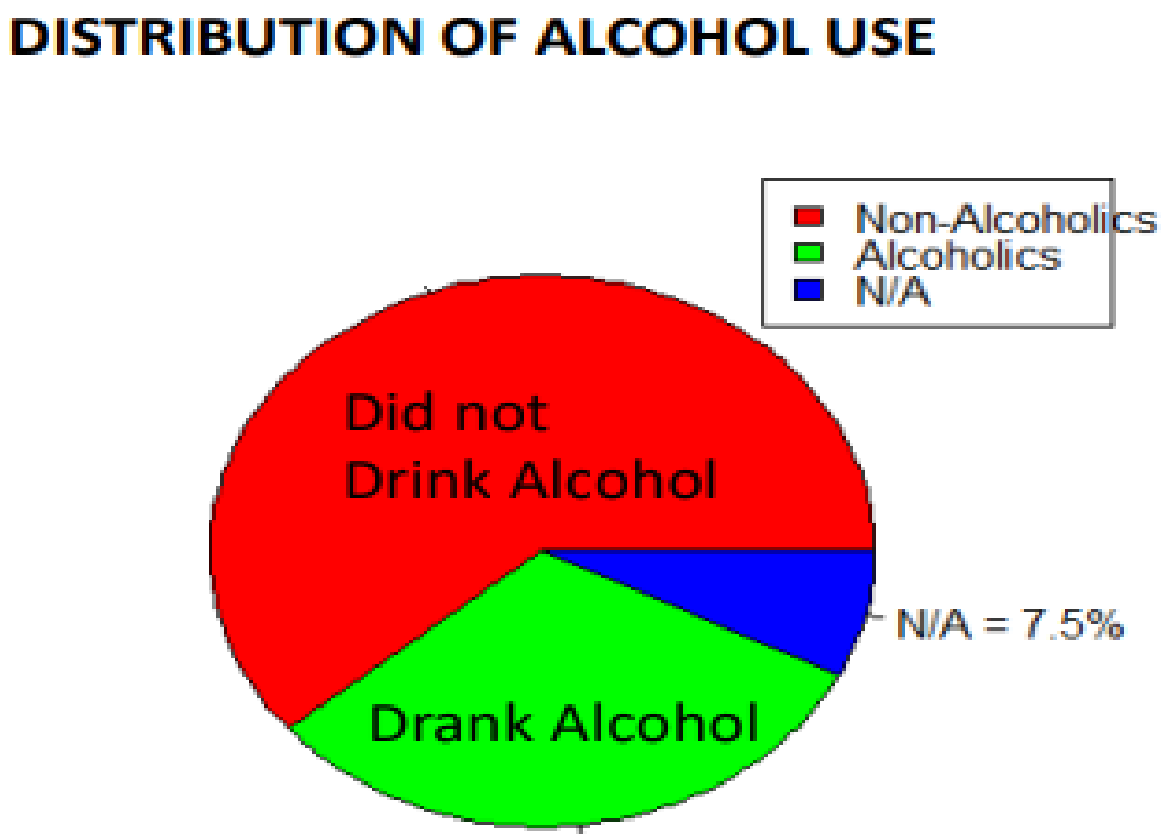

FIG 4.12 DISTRIBUTION OF ALCOHOL INTAKE

4.3.1 Determinants of Prostate Cancer Disease Severity Inherent to the Disease at Diagnosis

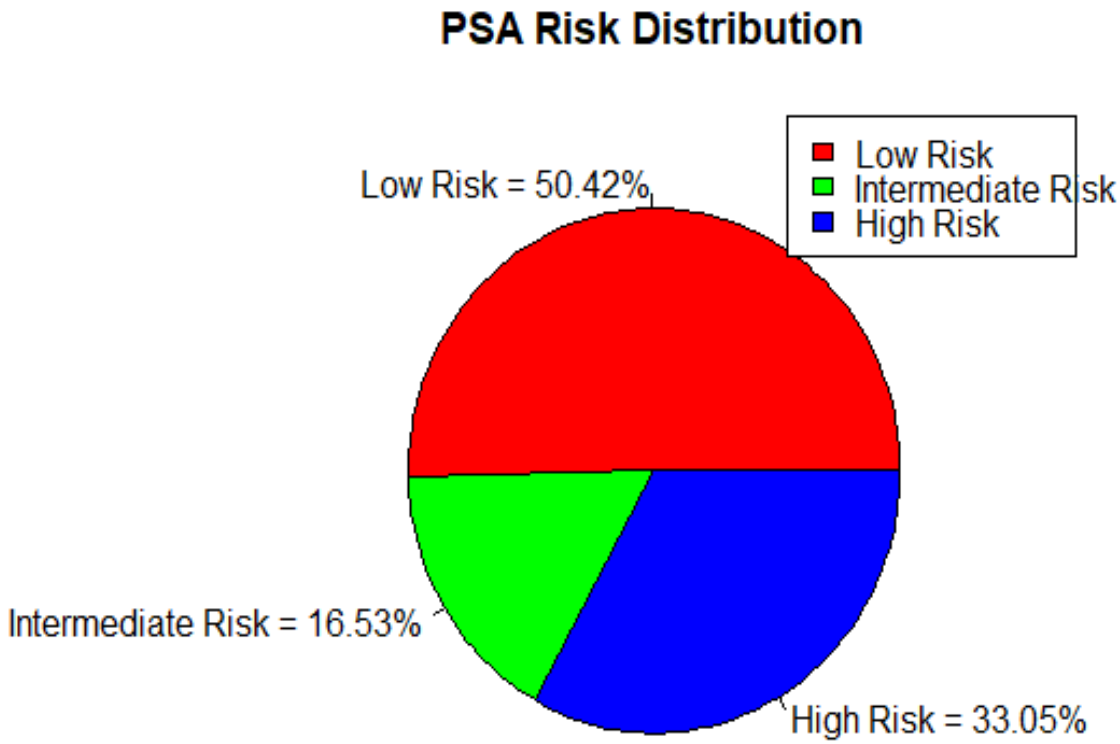

FIG 4.14 PSA RISK STRATIFICATION OF DISEASE

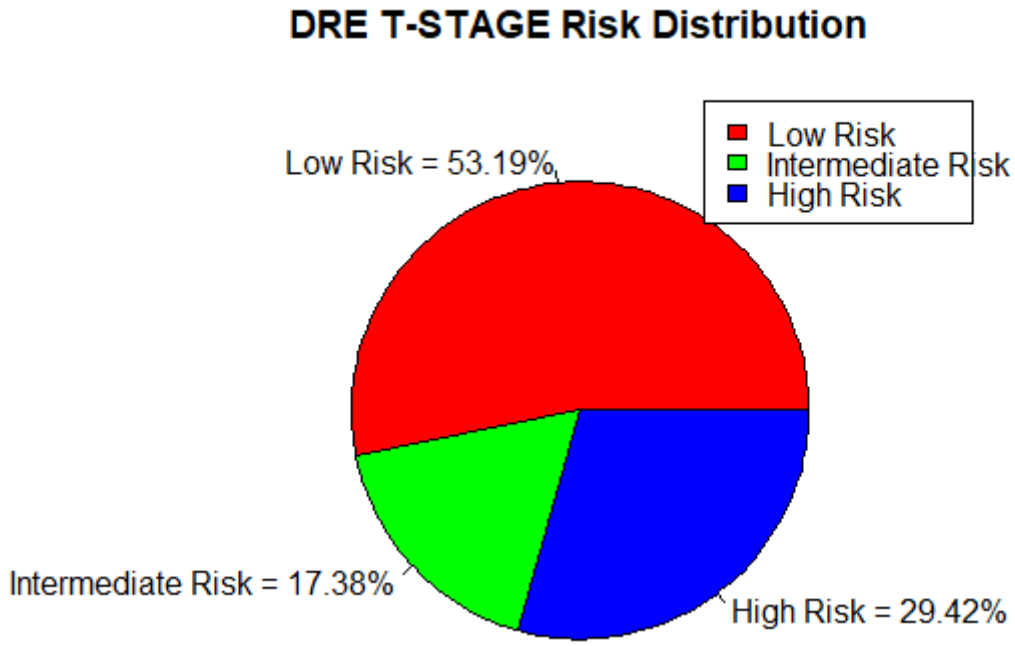

FIGURE 4.15 DRE RISK STRATIFICATION OF THE DISEASE

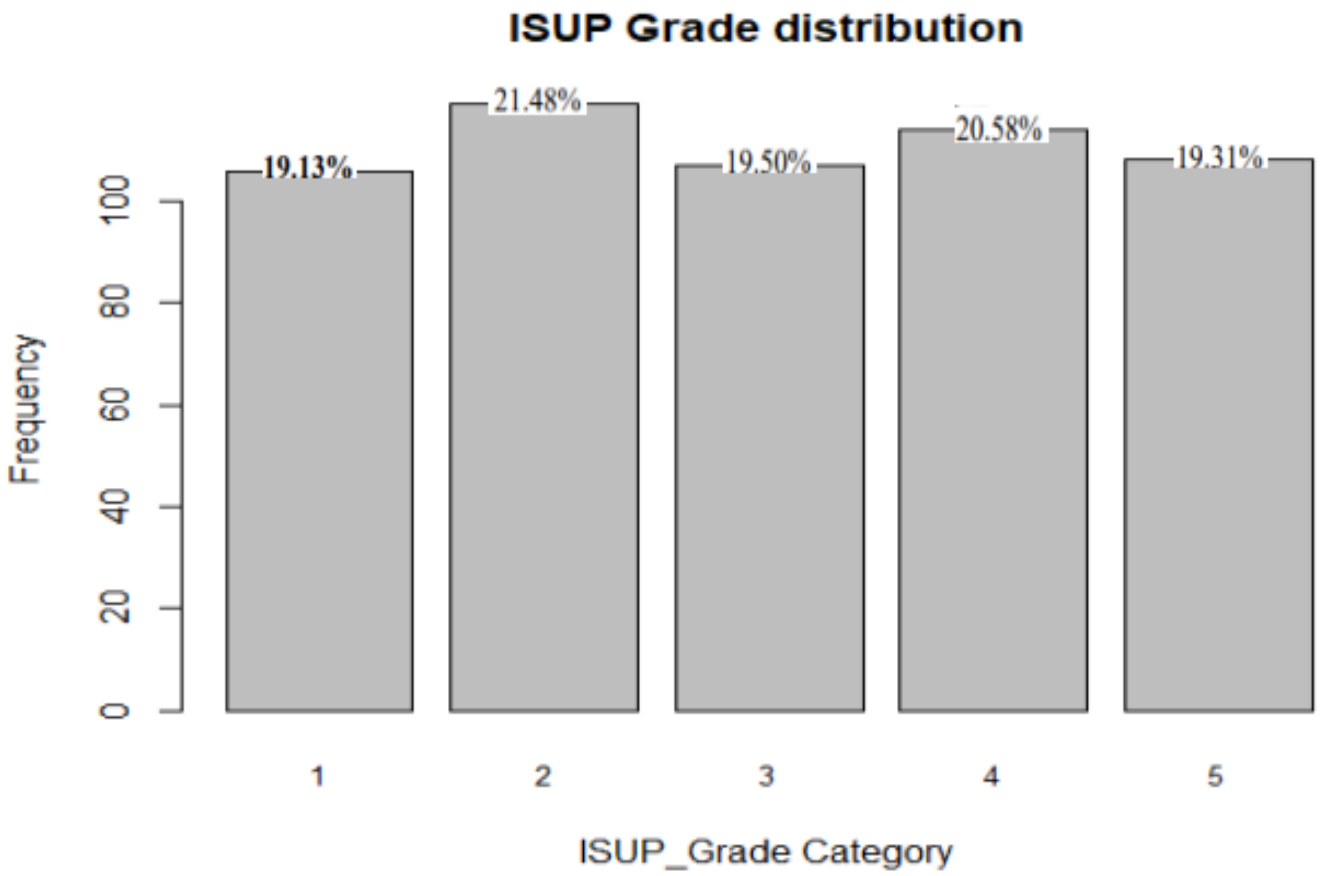

FIG 4.16 ISUP GRADING OF CASES IN OUR STUDY GROUP

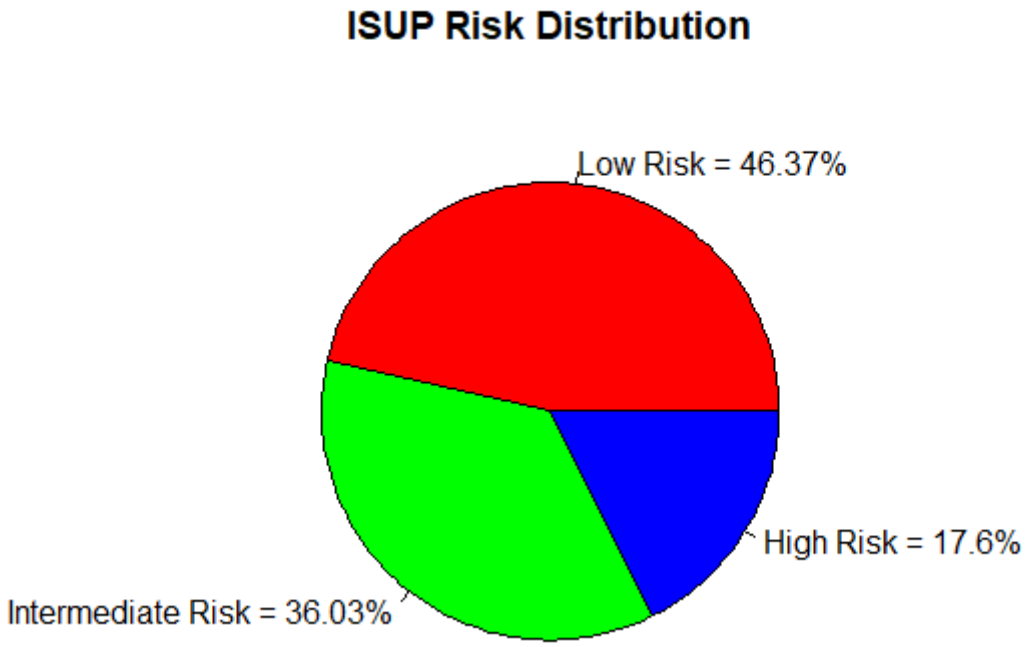

FIG 4.17 ISUP RISK STRATIFICATION OF THE PROSTATE CANCER CASES IN THE STUDY GROUP

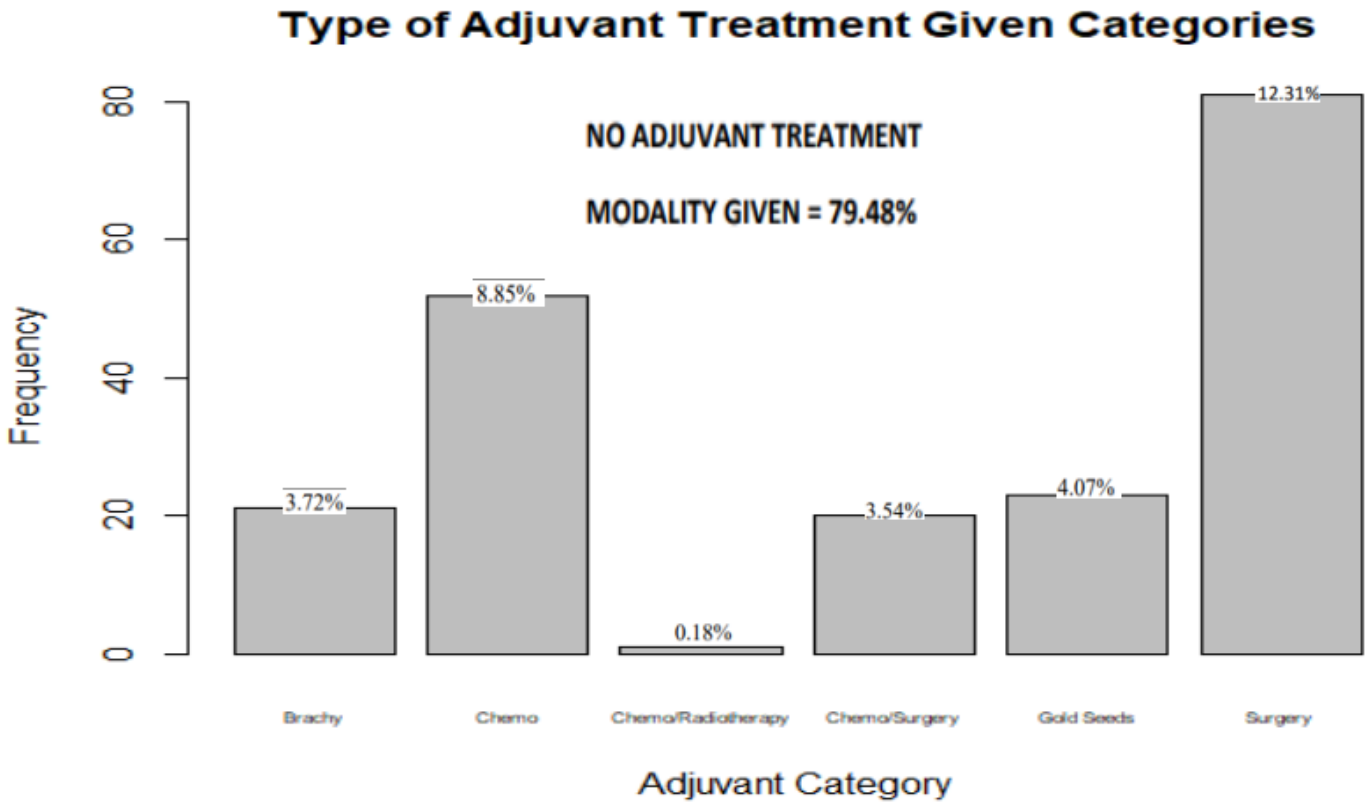

FIG 4.21 TYPES OF ADJUVANT THERAPY GIVEN TO THE PATIENTS

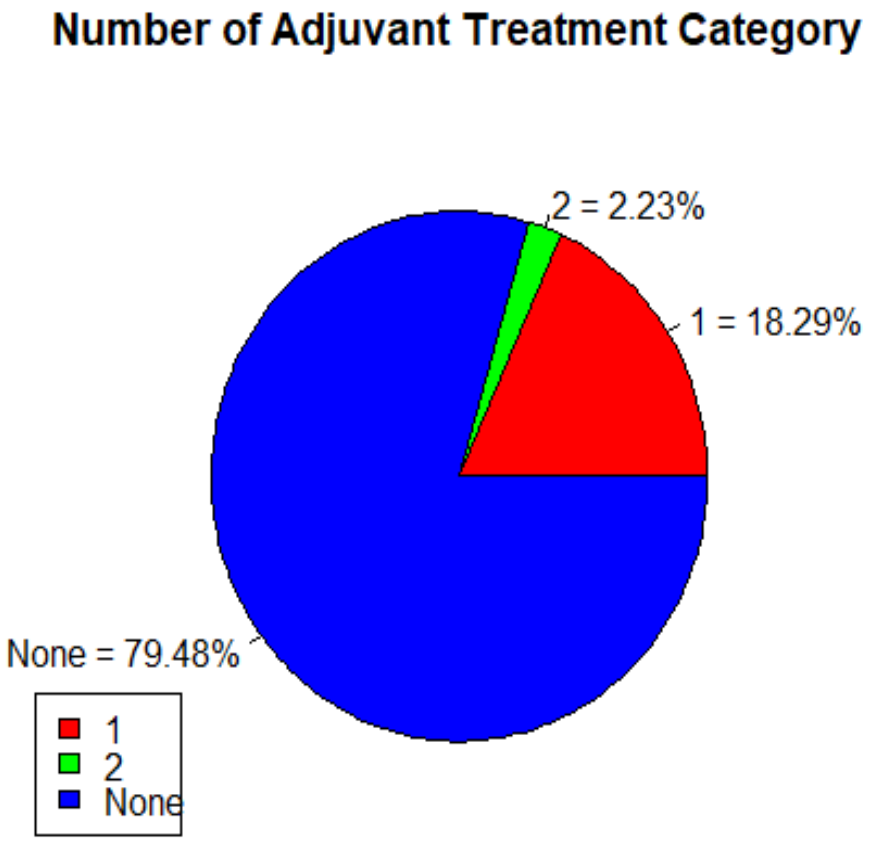

FIG 4.22 NUMBER OF ADJUVANT THERAPY RECEIVED

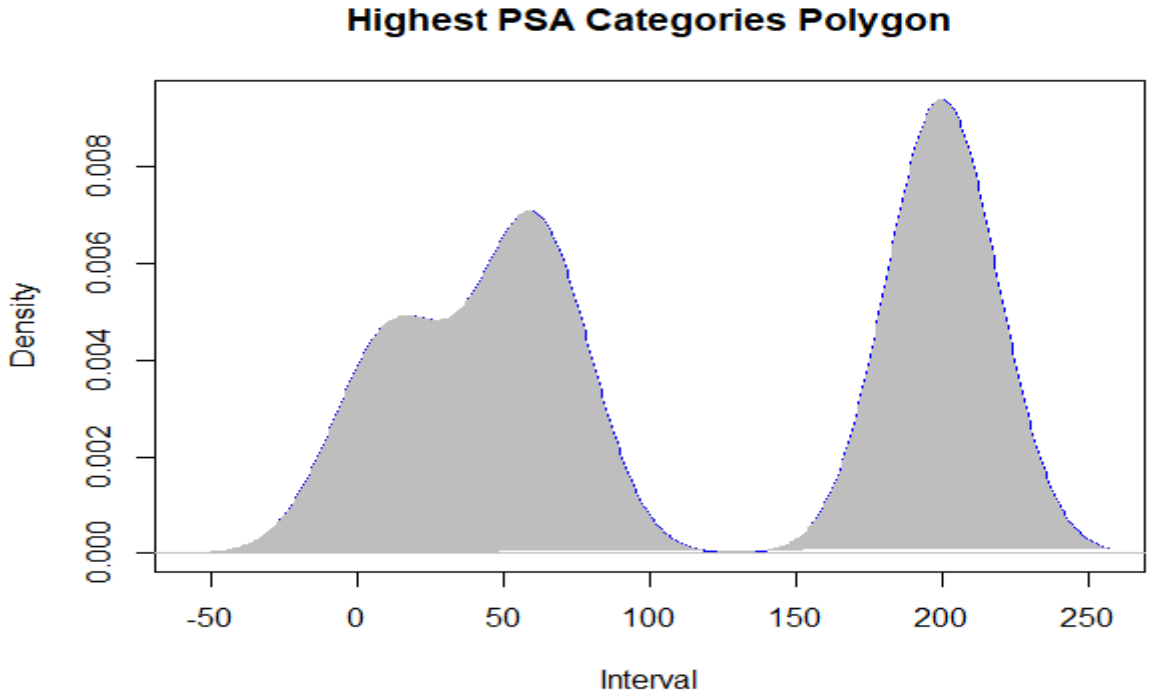

FIG 4.23 HIGHEST PSA VALUE DURING TREATMENT PERIOD

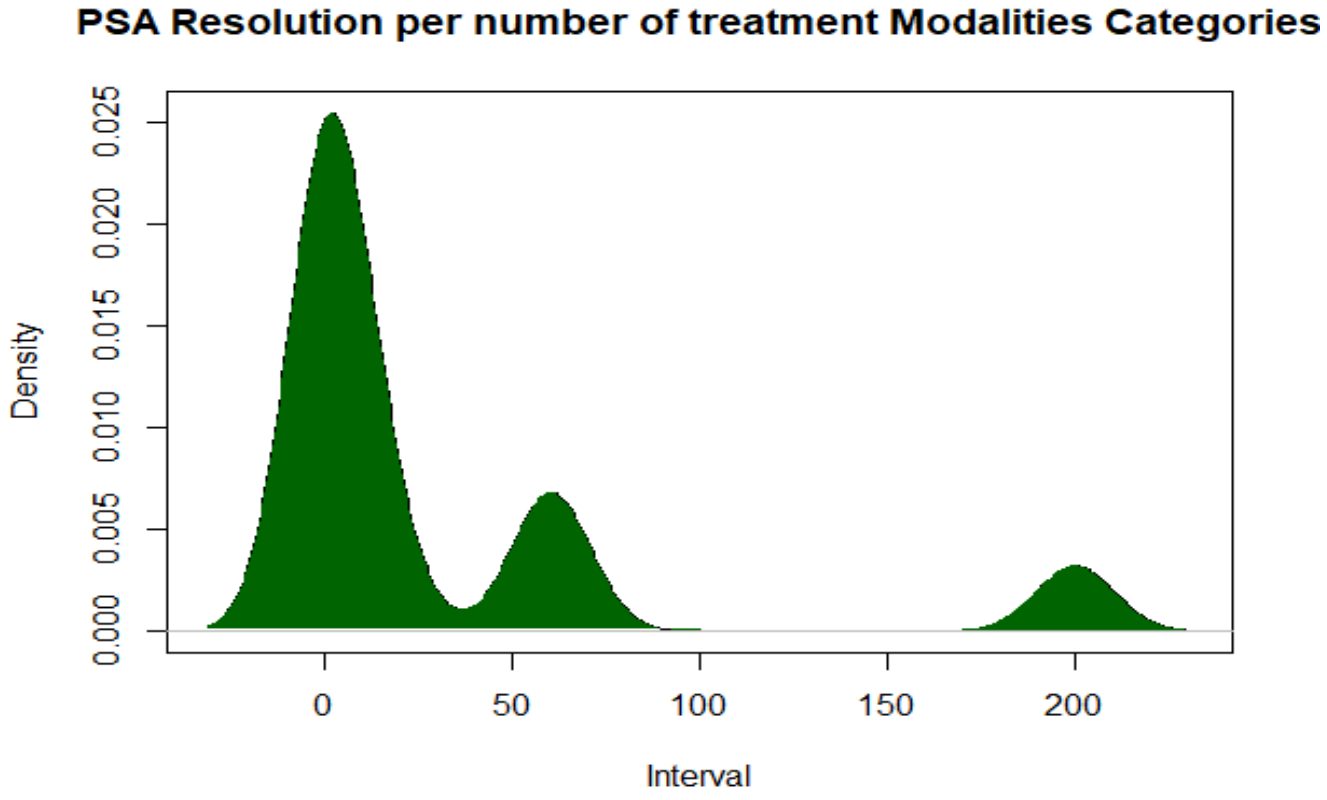

FIG 4.25 TREATMENT OUTCOME MEASURE RPSA PER MODALITY GIVEN; CATEGORIES

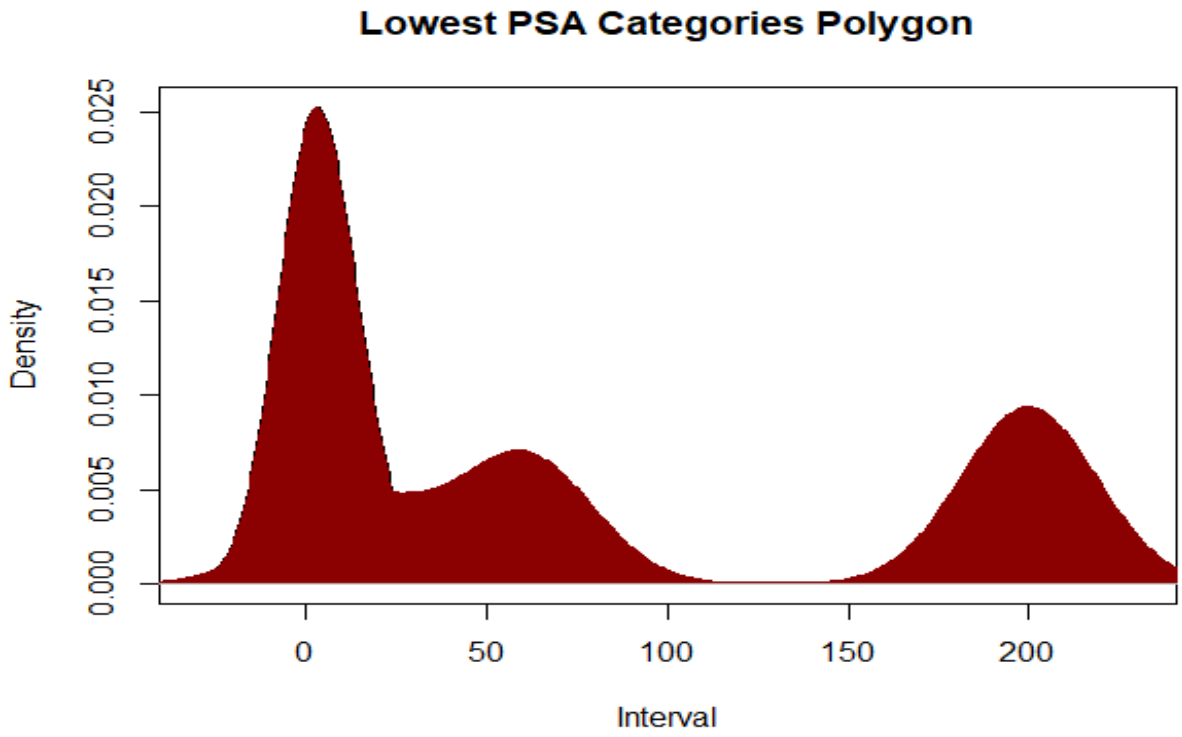

FIG 4.26 TREATMENT OUTCOME MEASURE: NADIR PSA CATEGORIES

Details of Calculations for the Test Of Difference between Proportions

For Akan Men:

1. **Given Data:**
   - Percentage with prostate cancer in the study (pSGMC) = 0.5552
   - Percentage of Akan men in Ghana (pGhana) = 0.475
   - Sample size of Ghanaian men attending SGMC Hospital with prostate cancer (nSGMC) = 776
   - Sample size of men in Ghana aged above 45 (nGhana) = 3,377,818
2. **Step 1: Calculate the Standard Error (SE):**
   - SE = √ [(pGhana * (1 - pGhana)) / nSGMC]
   - SE = √ [(0.475 * (1 - 0.475)) / 776]
   - SE ≈ 0.0062
3. **Step 2: Calculate the Test Statistic (Z):**
   - Z = (pSGMC - pGhana) / SE
   - Z = (0.5552 - 0.475) / 0.0062
   - Z ≈ 12.8968
4. **Step 3: Calculate the P-value:**
   - Using the Z-score, you can find the p-value from a standard normal distribution table or calculator. The p-value is much smaller than 0.05, so you reject the null hypothesis.
5. **Step 4: Set the Significance Level:**
   - Significance level = 0.05
6. **Step 5: Make a Decision:**

- We reject the null hypothesis, suggesting a statistically significant difference between the proportion of Akan men with prostate cancer attending SGMC Hospital and the percentage of Akan men among men in Ghana aged above 45.

Summary for Ga Men, Ewe Men, and Northern Ghanaian Men:

For Ga Men:

- Calculated Standard Error (SE) ≈ 0.0086
- Calculated Test Statistic (Z) ≈ 8.7209
- Calculated P-value is much smaller than 0.05, so you reject the null hypothesis.
- Conclusion: There is a statistically significant difference between the proportion of Ga men with prostate cancer attending SGMC Hospital and the percentage of Ga men among men in Ghana aged above 45.

For Ewe Men:

- Calculated Standard Error (SE) ≈ 0.0071
- Calculated Test Statistic (Z) ≈ -0.7752
- Calculated P-value is greater than 0.05, so you fail to reject the null hypothesis.
- Conclusion: There isn't enough evidence to conclude a statistically significant difference between the proportion of Ewe men with prostate cancer attending SGMC Hospital and the percentage of Ewe men among men in Ghana aged above 45.

For Northern Ghanaian Men:

- Calculated Standard Error (SE) ≈ 0.0077
- Calculated Test Statistic (Z) ≈ -34.6519
- Calculated P-value is much smaller than 0.05, so you reject the null hypothesis.
- Conclusion: There is a statistically significant difference between the proportion of Northern Ghanaian men with prostate cancer attending SGMC Hospital and the percentage of Northern Ghanaian men among men in Ghana aged above 45.

Table A1: Regression Analysis: Summaries

Characteristic	OR	95% CI	p-value
Ethnic group			
Akan	—	—	—
Ewe	0.86	0.53, 1.36	0.519
GA	0.72	0.43, 1.18	0.208
Northern	0.98	0.49, 1.89	0.961
Nigeria	0.57	0.20, 1.51	0.263
Togolese/Beninois	0.62	0.09, 2.89	0.575
Other West-Africa/Africa	0.58	0.12, 2.10	0.440
Asian/Caucasian	3,064,688	0.00, NA	0.981
Nationality			
Ghanaian	—	—	—
Nigerian			
Togolese/Beninois			
Other West-Africa/Africa			
Asian/Caucasian			

Place of residence			
Peri-urban	—	—	—
Rural	1.14	0.42, 3.18	0.801
Urban	0.82	0.39, 1.86	0.619
Marital Status			
Married	—	—	—
Single	1.38	0.79, 2.35	0.245
Divorced/Separated	0.65	0.21, 1.65	0.397
Widowed	0.78	0.29, 1.83	0.582
Physical activity occupation			
Non-rigorous occupation	—	—	—
Retired	1.53	0.82, 2.82	0.173
Rigorous-Activity occupation	1.48	0.99, 2.21	0.056
Occupation (SES)			
High SES	—	—	—
Low SES	0.62	0.42, 0.93	0.021
BMI levels			
Underweight	—	—	—
Normal	0.63	0.30, 1.34	0.218
Overweight	0.64	0.32, 1.32	0.220
Obese	0.35	0.13, 0.87	0.026
Morbidly Obese	0.63	0.25, 1.56	0.318
History of drinking alcohol			
No	—	—	—
Yes	1.31	0.89, 1.90	0.166
History of smoking tobacco			
No	—	—	—
Yes	1.02	0.53, 1.93	0.945
Family history of prostate cancer			
No	—	—	—
Yes	0.92	0.61, 1.37	0.677
Presence of comorbidity			
No	—	—	—
Yes	0.59	0.38, 0.89	0.014

Table A2: Iteration from the Results Section

PSATM						
AGE_CD	-2.006442	29.10527	-0.07	0.945	-59.23161	55.21872
MAR_CD	8.199752	22.12898	0.37	0.711	-35.30903	51.70853
ETH_CD	-8.875381	19.16247	-0.46	0.644	-46.55157	28.80081
SES	-5.731794	49.88634	-0.11	0.909	-103.8156	92.35197
ACT	37.86609	41.43999	0.91	0.361	-43.61093	119.3431
W	2.130367	2.766372	0.77	0.442	-3.30872	7.569454
H	-1.383486	1.736837	-0.80	0.426	-4.798358	2.031387
BMI	-13.70087	7.375459	-1.86	0.064	-28.20209	.8003458
BMI_CD	26.11871	50.9726	0.51	0.609	-74.1008	126.3382
FMH	-53.93115	57.34914	-0.94	0.348	-166.6879	58.82556
ALC	44.72897	55.91139	0.80	0.424	-65.20091	154.6589
TBC	76.93086	89.51486	0.86	0.391	-99.06831	252.93
LOC_CD	29.41942	26.39642	1.11	0.266	-22.47977	81.31861
DRE_CD	-22.17412	51.06362	-0.43	0.664	-122.5726	78.22436
PSA	.9141261	.0264017	34.62	0.000	.8622165	.9660357
ISUP	-21.08416	18.42362	-1.14	0.253	-57.30766	15.13935
MET_CD	-10.94641	94.62004	-0.12	0.908	-196.9831	175.0903
_cons	-2.079948	238.7704	-0.01	0.993	-471.5372	467.3773
PSAD_CD						
AGE_CD	.1707746	.093542	1.83	0.069	-.0131425	.3546917
MAR_CD	-.0826838	.0711208	-1.16	0.246	-.2225175	.0571499
ETH_CD	.0572717	.0615866	0.93	0.353	-.0638166	.1783599
SES	.1852897	.1603307	1.16	0.249	-.1299437	.500523
ACT	-.057363	.1331848	-0.43	0.667	-.3192236	.2044977
W	.0145005	.0088909	1.63	0.104	-.0029803	.0319813
H	-.008266	.0055821	-1.48	0.139	-.0192411	.0027092
BMI	-.0341301	.0237041	-1.44	0.151	-.0807358	.0124757
BMI_CD	-.0824716	.1638218	-0.50	0.615	-.404569	.2396259
FMH	-.0340787	.1843155	-0.18	0.853	-.3964697	.3283124
ALC	-.1181847	.1796947	-0.66	0.511	-.4714905	.2351212
TBC	-.0184772	.2876936	-0.06	0.949	-.5841244	.54717
LOC_CD	-.114825	.084836	-1.35	0.177	-.2816248	.0519748
DRE_CD	-.1746839	.1641144	-1.06	0.288	-.4973565	.1479888
PSA	.0004013	.0000849	4.73	0.000	.0002345	.0005681
ISUP	.1755442	.059212	2.96	0.003	.0591248	.2919637
MET_CD	.9092004	.3041012	2.99	0.003	.3112933	1.507107
_cons	1.831997	.767389	2.39	0.017	.3231986	3.340795

Table A3: Logistic Regression Output for Treatment Outcome variables

RPSA_CD

AGE_CD	.1015813	.0888156	1.14	0.253	-.0730429	.2762056
MAR_CD	-.057905	.0675272	-0.86	0.392	-.1906733	.0748632
ETH_CD	-.0156132	.0584748	-0.27	0.790	-.1305832	.0993568
SES	.2295241	.1522296	1.51	0.132	-.0697813	.5288295
ACT	-.1076569	.1264553	-0.85	0.395	-.3562863	.1409726
W	.0133822	.0084417	1.59	0.114	-.0032154	.0299797
H	-.0042594	.0053	-0.80	0.422	-.01468	.0061612
BMI	-.043057	.0225064	-1.91	0.056	-.0873079	.0011939
BMI_CD	-.0786293	.1555444	-0.51	0.613	-.384452	.2271935
FMH	-.2827604	.1750026	-1.62	0.107	-.6268407	.06132
ALC	-.1712608	.1706152	-1.00	0.316	-.506715	.1641934
TBC	.2510426	.2731572	0.92	0.359	-.286024	.7881091
LOC_CD	-.0220248	.0805494	-0.27	0.785	-.1803967	.136347
DRE_CD	.1241686	.1558221	0.80	0.426	-.1822002	.4305375
PSA	.0003517	.0000806	4.37	0.000	.0001933	.0005101
ISUP	.1661323	.0562202	2.96	0.003	.0555952	.2766693
MET_CD	.3458629	.2887358	1.20	0.232	-.2218335	.9135592
_cons	2.720984	.7286149	3.73	0.000	1.288422	4.153546

PSAD

AGE_CD	-2.401702	34.27044	-0.07	0.944	-69.78235	64.97894
MAR_CD	-18.61179	26.0561	-0.71	0.475	-69.84187	32.61829
ETH_CD	-12.97376	22.56314	-0.57	0.566	-57.33616	31.38864
SES	-40.67078	58.73943	-0.69	0.489	-156.161	74.81944
ACT	66.67942	48.79415	1.37	0.173	-29.25694	162.6158
W	.5058682	3.257306	0.16	0.877	-5.898468	6.910204
H	-1.964695	2.045065	-0.96	0.337	-5.985589	2.056199
BMI	-19.40242	8.684347	-2.23	0.026	-36.4771	-2.327736
BMI_CD	79.85432	60.01846	1.33	0.184	-38.15068	197.8593
FMH	-26.75807	67.52662	-0.40	0.692	-159.5252	106.009
ALC	39.56969	65.83371	0.60	0.548	-89.86892	169.0083
TBC	43.66736	105.4006	0.41	0.679	-163.5655	250.9003
LOC_CD	-3.292684	31.08087	-0.11	0.916	-64.40217	57.81681
DRE_CD	21.75541	60.12564	0.36	0.718	-96.46031	139.9711
PSA	.1019997	.0310871	3.28	0.001	.0408779	.1631214
ISUP	-3.847381	21.69317	-0.18	0.859	-46.4993	38.80454
MET_CD	45.39827	111.4118	0.41	0.684	-173.6535	264.45
_cons	184.6485	281.1439	0.66	0.512	-368.1211	737.4181

Table A4: Logistic Regression Output for Treatment Outcome variables

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	Coefficient	Std. err.	t	P>|t|	[95% conf.	interval]
FRM_CD						
AGE_CD	.0589448	.0378986	1.56	0.121	-.0155694	.133459
MAR_CD	.0332282	.0288146	1.15	0.250	-.0234256	.089882
ETH_CD	.0099437	.0249519	0.40	0.690	-.0391153	.0590027
SES	-.0291388	.0649581	-0.45	0.654	-.1568559	.0985782
ACT	.038068	.0539599	0.71	0.481	-.068025	.1441611
W	.0014795	.0036022	0.41	0.682	-.0056029	.0085618
H	-.0018362	.0022616	-0.81	0.417	-.0062828	.0026104
BMI	-.003011	.0096038	-0.31	0.754	-.0218934	.0158714
BMI_CD	-.0288453	.0663726	-0.43	0.664	-.1593434	.1016528
FMH	-.0602732	.0746756	-0.81	0.420	-.2070963	.0865498
ALC	-.0047989	.0728035	-0.07	0.947	-.147941	.1383433
TBC	.0659687	.1165593	0.57	0.572	-.1632037	.2951412
LOC_CD	-.0158214	.0343714	-0.46	0.646	-.0834005	.0517577
DRE_CD	.5201971	.0664911	7.82	0.000	.389466	.6509282
PSA	.0000228	.0000344	0.66	0.507	-.0000448	.0000904
ISUP	-.0189221	.0239898	-0.79	0.431	-.0660896	.0282453
MET_CD	-.9517144	.1232069	-7.72	0.000	-1.193957	-.7094718
_cons	.4300476	.3109083	1.38	0.167	-.1812432	1.041338
PSATM_CD						
AGE_CD	.1157491	.0880714	1.31	0.190	-.0574119	.2889102
MAR_CD	-.0505559	.0669614	-0.75	0.451	-.1822117	.0811
ETH_CD	.0064833	.0579849	0.11	0.911	-.1075234	.1204899
SES	.2501645	.1509541	1.66	0.098	-.0466331	.5469621
ACT	-.117107	.1253958	-0.93	0.351	-.3636532	.1294392
W	.0124995	.0083709	1.49	0.136	-.0039589	.028958
H	-.0030971	.0052556	-0.59	0.556	-.0134303	.0072362
BMI	-.039997	.0223178	-1.79	0.074	-.0838771	.0038831
BMI_CD	-.0838674	.1542411	-0.54	0.587	-.3871276	.2193929
FMH	-.2388527	.1735362	-1.38	0.170	-.5800501	.1023446
ALC	-.1659994	.1691856	-0.98	0.327	-.4986428	.1666441
TBC	.2349142	.2708684	0.87	0.386	-.2976523	.7674807
LOC_CD	-.0331923	.0798745	-0.42	0.678	-.1902371	.1238526
DRE_CD	.0766937	.1545165	0.50	0.620	-.2271082	.3804955
PSA	.0003569	.0000799	4.47	0.000	.0001998	.000514
ISUP	.1458442	.0557491	2.62	0.009	.0362333	.2554551
MET_CD	.4926677	.2863165	1.72	0.086	-.0702719	1.055607
_cons	2.588136	.7225099	3.58	0.000	1.167577	4.008695

Table A5: Logistic Regression Output for Treatment Outcome variables

RPSA

AGE_CD	3.067899	33.14802	0.09	0.926	-62.10591	68.24171
MAR_CD	4.712823	25.20272	0.19	0.852	-44.83938	54.26502
ETH_CD	-7.147387	21.82416	-0.33	0.743	-50.05684	35.76207
SES	-20.25802	56.81561	-0.36	0.722	-131.9657	91.44969
ACT	71.84873	47.19605	1.52	0.129	-20.94555	164.643
W	.1720734	3.150624	0.05	0.956	-6.022509	6.366656
H	-1.486746	1.978085	-0.75	0.453	-5.375949	2.402456
BMI	-17.68221	8.399919	-2.11	0.036	-34.19767	-1.166758
BMI_CD	73.83393	58.05275	1.27	0.204	-40.30619	187.9741
FMH	-42.19729	65.315	-0.65	0.519	-170.616	86.22146
ALC	44.00196	63.67754	0.69	0.490	-81.19731	169.2012
TBC	92.49645	101.9486	0.91	0.365	-107.9492	292.9421
LOC_CD	19.20904	30.06292	0.64	0.523	-39.89901	78.31708
DRE_CD	2.724728	58.15642	0.05	0.963	-111.6192	117.0687
PSA	.9613278	.030069	31.97	0.000	.9022078	1.020448
ISUP	-14.60611	20.98268	-0.70	0.487	-55.8611	26.64889
MET_CD	-9.409311	107.7629	-0.09	0.930	-221.2867	202.4681
_cons	15.57919	271.9359	0.06	0.954	-519.0862	550.2446

Summary of Iteration for the Prostate Cancer Case-Detection Models (Multivariate, and PSA alone)

Tables A6

```
. mvreg DIAG = PSA  TBC ALC FMH PND_CD LIN_CD BMI_CD SES ACT ETH_CD MAR_CD AGE_C
> D
```

Equation	Obs	Parms	RMSE	"R-sq"	F	P>F
DIAG	1,662	13	.4106284	0.3304	67.80087	0.0000

DIAG	Coefficient	Std. err.	t	P>|t|	[95% conf.	interval]
PSA	.0000353	7.03e-06	5.02	0.000	.0000215	.0000491
TBC	-.1934239	.0313108	-6.18	0.000	-.254837	-.1320108
ALC	-.0062649	.0230015	-0.27	0.785	-.0513801	.0388503
FMH	.1201369	.0268091	4.48	0.000	.0675535	.1727203
PND_CD	-.014591	.018012	-0.81	0.418	-.0499197	.0207378
LIN_CD	.0891567	.0225231	3.96	0.000	.0449799	.1333336
BMI_CD	-.0518322	.0233596	-2.22	0.027	-.0976498	-.0060145
SES	.1866324	.0177097	10.54	0.000	.1518965	.2213683
ACT	-.1870126	.0176599	-10.59	0.000	-.2216507	-.1523744
ETH_CD	-.0348008	.0066045	-5.27	0.000	-.0477549	-.0218468
MAR_CD	.0847508	.00779	10.88	0.000	.0694715	.1000301
AGE_CD	.1188849	.009464	12.56	0.000	.1003221	.1374477
_cons	-.0144959	.0529464	-0.27	0.784	-.1183453	.0893534

```
. discrim logistic AGE_CD MAR_CD ETH_CD SES ACT BMI_CD LIN_CD PND_CD FMH ALC PSA
> , group(DIAG)

Iteration 0:   log likelihood = -1151.4799
Iteration 1:   log likelihood = -858.82574
Iteration 2:   log likelihood =  -824.3851
Iteration 3:   log likelihood =  -806.3268
Iteration 4:   log likelihood = -788.73264
Iteration 5:   log likelihood = -762.82248
Iteration 6:   log likelihood = -704.60563
Iteration 7:   log likelihood = -650.02536
Iteration 8:   log likelihood = -633.18768
Iteration 9:   log likelihood = -631.42032
Iteration 10:  log likelihood = -631.40271
Iteration 11:  log likelihood = -631.40271


. mvreg DIAG = PSA

Equation             Obs    Parms        RMSE    "R-sq"          F       P>F
------------------------------------------------------------------------------
DIAG               1,662        2    .495841    0.0171   28.91838    0.0000

------------------------------------------------------------------------------
        DIAG | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
         PSA |   .0000455   8.46e-06     5.38   0.000     .0000289    .0000621
       _cons |   .5032606   .0122869    40.96   0.000     .4791611    .5273601
------------------------------------------------------------------------------

. discrim logistic PSA, group(DIAG)

Iteration 0:   log likelihood = -1151.4799
Iteration 1:   log likelihood = -1132.7674
Iteration 2:   log likelihood = -1109.2553
Iteration 3:   log likelihood = -1087.4156
Iteration 4:   log likelihood = -1061.6126
Iteration 5:   log likelihood = -1016.7566
Iteration 6:   log likelihood = -930.75092
Iteration 7:   log likelihood = -876.01163
Iteration 8:   log likelihood =  -860.8844
Iteration 9:   log likelihood = -859.95363
Iteration 10:  log likelihood = -859.95077

Logistic discriminant analysis
Resubstitution classification summary

        Key
  ------------
    Number
    Percent

           |  Classified
 True DIAG |         0          1 |     Total
-----------+----------------------+----------
         0 |       648        162 |       810
           |     80.00      20.00 |    100.00
           |                      |
         1 |       290        562 |       852
           |     34.04      65.96 |    100.00
-----------+----------------------+----------
     Total |       938        724 |     1,662
           |     56.44      43.56 |    100.00
           |                      |
    Priors |    0.5000     0.5000 |
```

```
. mvreg MET_CD = PSA

Equation             Obs    Parms        RMSE    "R-sq"          F       P>F
MET_CD               852        2    .4411491    0.0523    46.90091    0.0000

------------------------------------------------------------------------------
      MET_CD | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
         PSA |    .000052   7.59e-06     6.85   0.000     .0000371    .0000669
       _cons |   .2673073   .0154001    17.36   0.000     .2370807     .297534
------------------------------------------------------------------------------
```

Summary of Confusion Matrix Tables:

Multiparametric Screening Model:

Classified	**True Diagnosis**		
	0	**1**	**Total**
0	648	162	810
Percentage	**80.00%**	**20.00%**	**100.00%**
1	290	562	852
Percentage	**34.04%**	**65.96%**	**100.00%**
Total	**34.04%**	**65.96%**	**100.00%**
Percentage	938	724	1,662
Priors	0.5000	0.5000	

PSA Alone Screening model:

Classified	**True Diagnosis**		
	0	**1**	**Total**
0	584	23	607
Percentage	**96.21%**	**3.79%**	**100.00%**
1	166	79	245
Percentage	**67.76%**	**32.24%**	**100.00%**
Total	750	102	852
Percentage	**88.03%**	**11.97%**	**100.00%**
Priors	0.5000	0.5000	

Metastasis detection model: MET_CD vs. MAR_CD, SES, ACT, BMI, DRE_CD, PSA, ISUP Model:

Classified	**True MET_CD**		
	0	**1**	**Total**
0	289	26	315
Percentage	**91.75%**	**8.25%**	**100.00%**
1	13	147	160
Percentage	**8.13%**	**91.88%**	**100.00%**
Total	302	173	475
Percentage	**63.58%**	**36.42%**	**100.00%**
Priors	0.5000	0.5000	

MET_CD vs. PSA Model:

Classified	True MET_CD		
	0	**1**	**Total**
0	584	23	607
Percentage	**96.21%**	**3.79%**	**100.00%**
1	166	79	245
Percentage	**67.76%**	**32.24%**	**100.00%**
Total	750	102	852
Percentage	**88.03%**	**11.97%**	**100.00%**
	Priors	0.5000	0.5000

These simplified tables above provide a clear overview of the confusion matrix results for each model.

Summary of Discriminatory Analysis Results (Percentages):

Model	Sensitivity	Specificity	Precision	Accuracy	F1-Score	AUC	Population Yield	Prevalence Yield
Multiparametric screening Model	91.75%	96.15%	96.15%	88.03%	91.75 %	64.19 %	68.54%	96.15%
PSA Alone screening Model	32.24%	96.15%	32.24%	88.03%	32.24 %	64.19 %	9.25%	32.24%
MET_CD vs. MAR_CD, SES, ACT, BMI, DRE_CD, PSA, ISUP	96.15%	32.24%	96.15%	88.03%	96.15 %	64.19 %	96.15%	68.54%
MET_CD vs. PSA	32.24%	96.15%	32.24%	88.03%	32.24 %	64.19 %	32.24%	9.25%

These results provide a concise summary of the discriminatory analysis metrics for each model, with all values presented as percentages.

⁎General Guidelines for High SES, and Low SES:

This is based on common socioeconomic classifications found in research. It's important to note that socioeconomic status (SES) is a multifaceted concept influenced by factors like income, education, and occupation.

High Socioeconomic Status (SES) Occupations:

1. **Physicians and Surgeons**: Occupations in the medical field, such as doctors and surgeons, are typically associated with high SES due to extensive education and earning potential (Smith et al., 2019).
2. **Lawyers**: Legal professionals, including lawyers and judges, often have high SES because of their advanced education and income (Johnson & Smith, 2018).

3. **Engineers**: Engineering professions generally command a high SES due to specialized knowledge and earning potential (Smith & Brown, 2020).
4. **Professors and Academics**: University professors and researchers are considered high SES due to their educational attainment and role in academia (Jones & Davis, 2017).
5. **Corporate Executives**: Top-level executives in large corporations often enjoy high SES because of their significant income and influence (Anderson et al., 2021).
6. **Dentists**: Dentists, like medical doctors, require extensive education and typically have high earning potential (White & Black, 2016).

Low Socioeconomic Status (SES) Occupations:

1. **Retail and Service Workers**: Jobs in retail, such as cashiers and sales clerks, and service industries like fast food or hospitality, are often associated with low SES due to lower wages (Brown & Johnson, 2019).
2. **Janitors and Cleaners**: Cleaning and maintenance jobs typically fall into the low SES category due to lower wages and less formal education (Smith & Davis, 2018).
3. **Agricultural Workers**: Farm laborers and agricultural workers often have lower SES due to physically demanding work and relatively lower wages (Jones et al., 2020).
4. **Factory Workers**: Assembly line and manufacturing jobs can be considered low SES, especially if they involve repetitive tasks and lower pay (Anderson & White, 2017).
5. **Unskilled Laborers**: Jobs that require minimal skills and education, such as general laborers and construction workers, are often associated with lower SES (Smith & Black, 2015).
6. **Food Service Workers**: Jobs in the food service industry, including dishwashers and fast food workers, are typically considered low SES due to lower wages and limited educational requirements (Brown et al., 2021).

These categories are influenced by regional variations and specific study methodologies.

∗General Guidelines for Sedentary and Non-sedentary Occupations:

Assigning occupations to sedentary or non-sedentary categories depends on the nature of the work involved. Below is a general guideline for categorizing some occupations based on their typical activity level.

Sedentary Occupations:

1. **Office Workers**: Occupations that primarily involve desk-based work, such as data entry, administrative tasks, and computer programming, are generally considered sedentary (Dunstan et al., 2012).
2. **Professional: Accountants, Lawyers, Doctors, Administrators, Civil Servants, Professors, Lecturers**: Accountants, etc; often spend most of their workday at a desk, reviewing financial data and preparing reports, which is predominantly sedentary work (Bauman et al., 2011).
3. **Writers and Editors**: Professionals in writing and editing roles typically engage in sedentary activities while working on manuscripts, articles, or content creation (Parry et al., 2013).
4. **Telemarketers**: Telemarketing jobs involve sitting for extended periods while making phone calls and handling customer inquiries, making them sedentary roles (Healy et al., 2013).

Non-Sedentary Occupations:

1. **Construction Workers**: Construction jobs involve physically demanding tasks like lifting, carrying, and operating heavy machinery, categorizing them as non-sedentary (Matthews et al., 2012).
2. **Nurses**: Nurses have physically active roles that include patient care, moving equipment, and walking within healthcare settings, classifying them as non-sedentary (Chen et al., 2015).

3. **Farmers**: Farming requires activities like planting, harvesting, and tending to livestock, making it a non-sedentary occupation (Bull et al., 2015).
4. **Retail Sales Associates**: Jobs in retail often involve standing, walking, and assisting customers, indicating a non-sedentary nature (Owen et al., 2012).
5. **Fitness Instructors, Sportsmen, Forces and Security agencies**: Fitness instructors lead exercise classes and, together with the underlisted, engage in physical activity themselves, making their work non-sedentary (Loprinzi et al., 2014).

These categories are generalized and may not cover every aspect of each occupation. Some roles within a category may have variations in activity level.

APPENDIX 5

Selection of Diagnostic Thresholds for the Models

The diagnostic threshold or cut-off risk value for each model will depend on the specific goal and context of the analysis, as well as the trade-offs between sensitivity and specificity that are acceptable in a given medical or diagnostic setting.

1. **Multiparametric screening Model:** This model achieves a balance between sensitivity and specificity. we may choose a cut-off risk value around 0.5 (50%) as the diagnostic threshold. This means that if the estimated risk of a positive diagnosis is above 50%, we would classify the patient as positive for the condition (and proceed to confirmatory tests), and below 50%, we would classify the patient as negative (and follow-up).
2. **PSA Alone Model:** This model has relatively low sensitivity but high specificity. To maximize specificity, we might choose a higher cut-off risk value, such as 0.8 (80%) or even higher. This would mean that a patient's estimated risk would need to be 80% or higher to classify them as positive.
3. **MET_CD vs. MAR_CD, SES, ACT, BMI, DRE_CD, PSA, ISUP Model:** Similar to the multiparametric screening model, a cut-off risk value around 0.5 (50%) will be chosen as reasonable threshold for this model, balancing sensitivity and specificity.
4. **MET_CD vs. PSA Model:** Like the PSA alone model, this model may benefit from a higher cut-off risk value to maximize specificity, perhaps around 0.8 (80%) or higher.

We also note that the choice of cut-off risk value will be made in consultation with the whole medical and public health teams and will consider the potential consequences of false positives and false negatives in the specific clinical or population context. The choice would also depend on the relative importance of sensitivity and specificity for the intended use of the model.

Ultimately, the diagnostic threshold would be carefully selected to align with the clinical/public health goals and risk tolerance of the healthcare provider or institution using the model.

DATA COLLECTING INSTRUMENT

Title: "Prostate Cancer Determinants, Disease Severity, and Treatment Outcomes at the Swedish Ghana Medical Center in the Greater Accra Region of Ghana," dated June 2023:

Data Collection Checklist - Prostate Cancer Study *(Date: March to June 2023)*

Demography:

1. ☐ ID Number: _____
2. ☐ Age: _____
3. ☐ Sex: _____
4. ☐ Occupation: _____
5. ☐ Educational Level: _____
6. ☐ Religion: _____
7. ☐ Marital Status: _____
8. ☐ Number of Children: _____
9. ☐ Ethnic Group: _____
10. ☐ Nationality: _____
11. ☐ Residence: _____
12. ☐ Alcohol Consumption: _____
13. ☐ Smoking Status: _____

Clinical Parameters:

14. Weight: _____
15. ☐ Height: _____
16. ☐ BMI (Body Mass Index): _____
17. ☐ Ponderex-Index: _____
18. ☐ Blood Pressure (BP): _____
19. ☐ Blood Sugar (if available): _____
20. ☐ Full Blood Count (CBC): _____
21. ☐ Liver Function Tests (LFTs): _____
22. ☐ Blood Urea and Creatinine (BUE and CR):
    _____
23. ☐ Initial PSA (Prostate-Specific Antigen):
    _____
24. ☐ Nadir PSA: _____
25. ☐ Current PSA: _____
26. ☐ Prostate Cancer Diagnosis (Provide in Full):
    _____
27. ☐ Stage of Disease: _____
28. ☐ Gleason Score of Histopathology: _____
29. ☐ Number of Cores with Cancer: _____
30. ☐ Percentage of Cores Affected: _____
31. ☐ Perineural Invasion: _____
32. ☐ Perivascular Invasion: _____
33. ☐ Lymph Node Involvement on CT Scan/MRI:
    _____
34. ☐ Liver Involvement on USG (Ultrasound):
    _____
35. ☐ Bone Scan Results: _____

36. Number of Metastatic Sites on Bone Scan:
_____
37. Digital Rectal Examination (DRE) Findings (if available):
_____
38. Treatment Modality/Modalities Employed:
_____
39. Number of Grays of EBRT (External Beam Radiation Therapy), in how many fractions, over how long?: _____
40. Presence or Absence of Lower Urinary Tract Symptoms:
_____
41. Catheter In-Situ (Already or Need for Catheter):
_____
42. Treatment Outcome (Cured/Remission/Progression/Recurrence/Adverse Events/SRE/Mortality):
_____

Family History:

43. Family History of Prostate Cancer: _____
44. Family History of Breast Cancer: _____
45. Family History of Bladder Cancer: _____
46. Family History of Other Cancers (Specify which cancer):
_____

History of other cancers in General:

47. Cancer in General (General information on medical history related to cancer):
_____

LETTERS OF CORRESPONDENCE

LETTER OF INTRODUCTION FROM ENSIGN GLOBAL COLLEGE TO SWEDEN GHANA MEDICAL CENTER

ENSIGN GLOBAL
COLLEGE

OUR REF: ENSIGN/AR/SN-230/ER003 Sept 9, 2023
YOUR REF:

The Chief Executive Officer
Sweden Ghana Medical Center
P.O. Box, MD 1879
Madina - Accra

Dear Sir,

LETTER OF INTRODUCTION

We respectfully write to introduce to you **Frank Obeng** (Student Identification number 227100230), a student of the Master of Public Health (MPH) degree program of the College.

As part of his graduation requirements, he is writing a thesis on the topic; **"Prostate Cancer Determinants, Disease Severity and Treatment Outcomes at a Medical Center in the Greater Accra Region of Ghana"** and would like to obtain data from your outfit.

We would be grateful if you kindly accede him any assistance he may require in the collection of this data in your unit for the thesis.

Thank you.

Respectfully yours,

Patrick Kums
Registrar

LETTER TO REQUEST FOR PERMISSION TO CONDUCT RESEARCH, WRITTEN TO THE SWEDEN GHANA MEDICAL CENTER

The Chief Executive Officer/Medical Director,

Sweden Ghana Medical Centre,

Accra – Ghana.

Thru' the Head of Clinical Department, SGMC,

Dr. Emmanuel Amankwaa-Frempong,

Accra – Ghana.

Dear Sir,

20th. March, 2023.

REQUEST FOR SECONDARY DATA FOR RESEARCH--''PROSTATE CANCER DETERMINANTS, DISEASE SEVERITY AND TREATMENT OUTCOMES AT A MEDICAL CENTRE IN THE GREATER ACCRA REGION OF GHANA''.

I am Dr. Frank Obeng, a (a Urologist at Ho Teaching Hospital, and a Lecturer at the University of Health and Allied Sciences, Ho, VR); and currently an MPH student (from Ensign Global College) on an Advanced Practicum Experience-Internship at your facility, SGMC, in Accra.

I have as part of this internship, written down the research protocol for a descriptive study on the topic: ''**PROSTATE CANCER DETERMINANTS, DISEASE SEVERITY AND TREATMENT OUTCOMES AT A MEDICAL CENTRE IN THE GREATER ACCRA REGION OF GHANA'**. (A copy is available for your perusal).

I write this letter of request for data, to obtain permission from your high office to enable me obtain data for the above research which will help improve public health outcomes in the area of cancer prevention and care. The research team at SGMC has duly made me sign the official form for ethical behaviour and ethical conduct in research, for this institution.

I hope that this permission shall be granted.

Sincerely yours,

Dr. Frank Obeng; MBChB, CEMBA, MGCPS, FGCS

Urologist and Lecturer,

MPH STUDENT AT ENSIGN GLOBAL COLLEGE, KPONG

(+233) 024 441 9607)

(fobeng@uhas.edu.gh; frankurology478@gmail.com)

cc: General Manager, SGMC

Sincerely yours.

ADMINISTRATIVE PERMISSION FROM STUDY SITE

SGMC CANCER CENTRE
SWEDEN GHANA MEDICAL CENTRE

P. O. Box MD 1879, Madina Accra
Tel: +233 307 032 133
+ 233 262 253 328
Email: info@sgmcltd.com
www: sgmccancercentre.com

The Chairperson,
Ghana Health Service Ethics Review Committee
Research And Development Division
P.O.Box, MB190
Accra.

Dear Sir,

Permission To Conduct Research- 'Prostate Cancer Disease Determinants, Severity and Treatment Outcomes at a Medical Center in the Greater Accra Region of Ghana'

We are pleased to inform you of our interest in the research topic **"PROSTATE CANCER DISEASE DETERMINANTS, SEVERITY AND TREATMENT OUTCOMES AT A MEDICAL CENTER IN THE GREATER ACCRA REGION OF GHANA'**; to be presented by Dr. Frank Obeng, We, therefore, approve of the study to be carried out.

We kindly request that the Review Board grant him any approval and ethical clearance needed to conduct the aforementioned study at our facility under academic supervision. We look forward to giving him all the necessary support to complete the work and wish him the best.

Sincerely,

DR. CLEMENT E. EDUSA
C. E. O.
SWEDEN GHANA MEDICAL CENTRE
P.O. BOX MD 1879, MADINA - ACCRA

Dr. Emmandel Amanikwaa Frempong
(Oncologist, Head of Clinical and Research Department)

Dr.Clement Edusa
(Oncologist and CEO SGMC)