Quality of evidence on prostate cancer in Nigeria

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Prostate cancer is the 2nd commonest malignancy in men worldwide. It is, however, the commonest in Nigeria. While several disparities have been documented between Caucasian men and men of African descent, there is limited research on prostate cancer in Nigeria. Evidence based medicine is a key tool in making clinical decisions and developing screening and treatment guidelines. This review was undertaken to assess the levels of evidence on prostate cancer research in Nigeria. A systematic review of all research published on prostate cancer from January 1975 to May 2018 in Nigeria was conducted. We reviewed all articles found on various databases by searching for "Prostate cancer in Nigeria". We classified them based on their study designs into different levels of evidence as well as year of publication. Meta-analyses were not considered in the review. A total of 171 articles were eligible for this review. Most publications were at the 4th (66%) and 5th levels of evidence (17%) respectively. No clinical trials on prostate cancer in Nigeria was seen or registered on clinicaltrials.gov, hence no studies at level 1 (a, b or c) of evidence published in Nigeria. The commonest type of study design was cross-sectional studies accounting for 56% of all publications. Prostate cancer research is currently at low levels of evidence in Nigeria. It is pertinent to explore and increase funding channels for cancer related research.

KEYWORDS: Prostate,cancer, Nigeria.

INTRODUCTION

In 2012, an estimated 14.1 million new cases of cancer were diagnosed worldwide. Prostate cancer was the second most prevalent malignancy in men after lung cancer worldwide. It is the fifth most common cause of cancer deaths (Ferlay et al., 2015). In Nigeria, it is the commonest malignancy in men and its incidence continues to rise (Elima et al., 2012; Adeloye et al., 2016). Globally, several disparities have been documented between Caucasian men and men of African descent. These include an increased risk of developing prostate cancer in Black men, younger age of incidence in Black men, and genetic differences. These factors might have an impact on survival outcomes (Odedina et al., 2009; Brawley, 2012). Prostate cancer management in African men is quite challenging as most patients present with metastatic disease (Shenoy et al. 2016).

Evidence-based medicine is a crucial tool in making clinical decisions and developing guidelines for management. (Burns, Rohrich, and Chung, 2011) Most screening and treatment guidelines used in different parts of the world for managing prostate cancer are formulated from evidence-based results obtained from mostly clinical trials and metanalyses on studies conducted in those countries. The National Institute for Health and Care Excellence (NICE) guidelines for treatment is predominantly based on research carried out in the United Kingdom (UK). A similar situation pertains regarding the National Comprehensive Cancer Network (NCCN) guidelines in the United States of America (USA). Evidence based medicine is a concept developed in the early 80s, then further described and modified by Sackett in 1989 (Sackett et al., 1996). It groups different studies based on their levels of evidence from one to five. Randomized controlled trials (RCT) and metanalyses are placed at the highest level of evidence, whilst, case series, case studies and expert opinions are at the lowest level. RCTs are structured to be unbiased; subjects are allocated randomly to two or more treatment groups whilst case series or expert opinion are associated with bias and based on writer's experience or opinions and there is often no control of confounding factors. The centre for evidence-based medicine in Oxford developed an adaptable tool to assess the levels of evidence in 2011 (Table 1). The tool is a hierarchical system of classifying based on evidence and designed for use by researchers.

Table 1: The Centre for Evidence-Based Medicine in Oxford published the levels of evidence in 2009, and modified in 2011(OCEBM Levels of Evidence Working Group et al. 2011)

Levels of Evidence for Therapeutic Studies[*]

Level	Type of evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow confidence intervals)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual Cohort study (including low quality RCT, e.g. <80% follow-up)
2C	"Outcomes" research; Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual Case-control study
4	Case series (and poor quality cohort and case-control study)
5	Expert opinion without explicit critical appraisal or based on physiology bench research or "first principles"

[*]From the Centre for Evidence-Based Medicine, http://www.cebm.net.

In Nigeria, prostate cancer prevention, screening, and clinical treatment modalities should be based on evidence-based research done or validated in Nigerian patients, in the expectation that this would lead to improved treatment outcomes and therefore survival. However, there are no publications exploring the levels of evidence in prostate cancer research in Nigeria. This review was done to explore levels of evidence on prostate cancer in Nigeria.

METHODS

We followed the Preferred Reporting for Systematic Reviews and Meta-Analyses (PRISMA) statement for the conduct of our systematic review (except that we did not consider metanalyses).
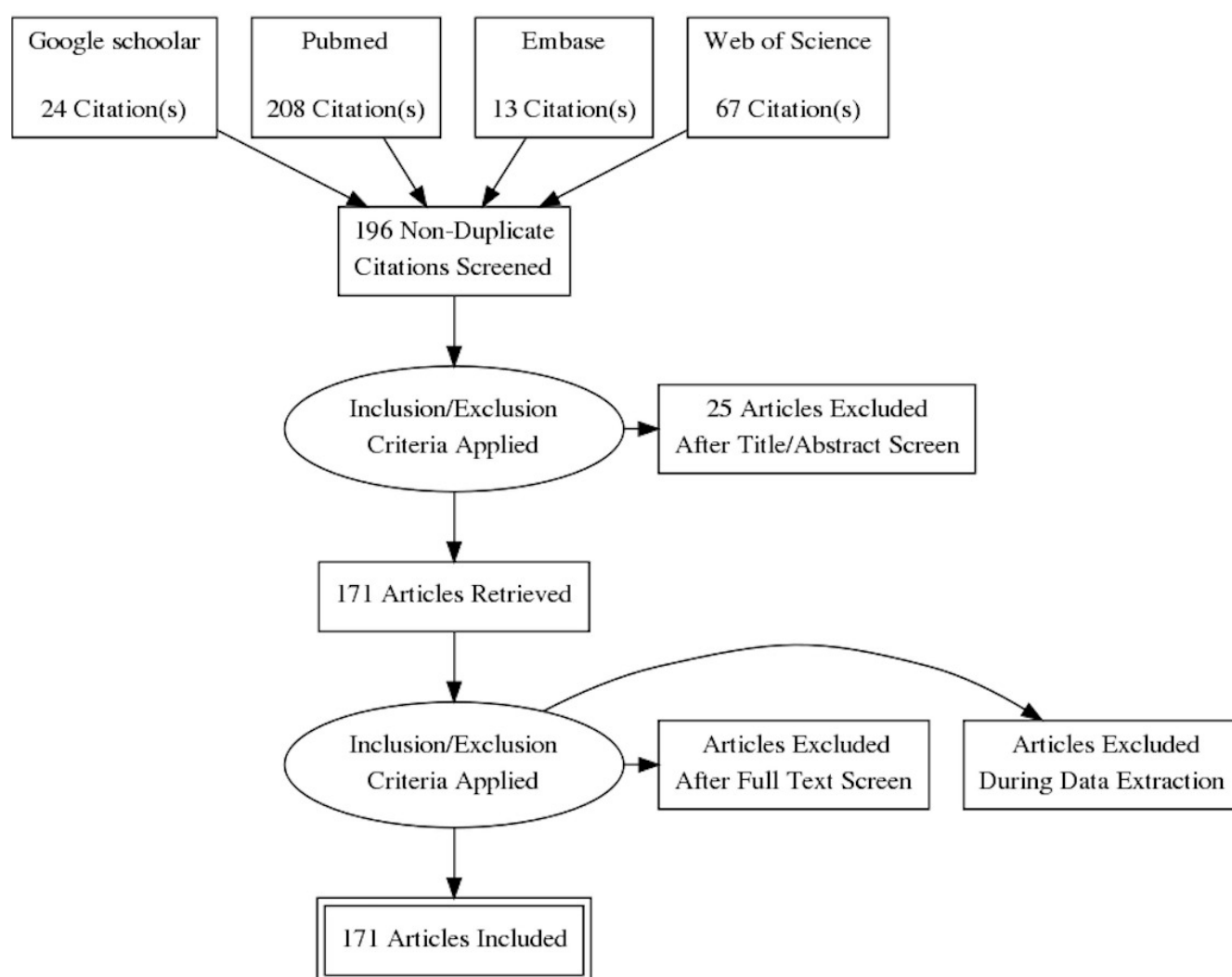

Figure 1: Illustrating the PRISMA selection criteria

STUDY SELECTION

An electronic literature search of all research published on prostate cancer from January 1975 to

May 2018 in Nigeria was conducted. We reviewed all articles found on PubMed, Web of Science, Embase, and Google Scholar search engines by searching "Prostate cancer in Nigeria". Using the PRISMA and National Institute of Health (NIH) guidelines, we reviewed and classified the articles based on their study designs into different levels of evidence. We included all studies on prostate cancer in Nigeria with either the full article or abstract having adequate information on the methodology of the study and excluded those with insufficient details. Information extracted from studies include the year of publications, study design, and level of evidence. Studies selected were grouped into five levels of evidence according to the Oxford Centre for Evidence-based Medicine classification (OCEBM Levels of Evidence Working Group et al. 2011). Meta-

analyses were not considered in the review due to varying study designs and difficulty in pooling them together.

EVIDENCE SYNTHESIS

During our search we identified 302 publications, 106 duplicates were removed and 25 were excluded based on inadequate information on the methodology of the study. A total of 171 articles were eligible for this review. Most studies published were cross sectional studies (56%), followed by cohort studies (15%), laboratory studies(13%), case reports (7%), expert opinion (3%), systematic reviews (2%) and meta-analysis (1%). There were no clinical trials on prostate cancer in Nigeria seen or registered on clinicaltrials.gov or other clinical trials registries (figure 2).
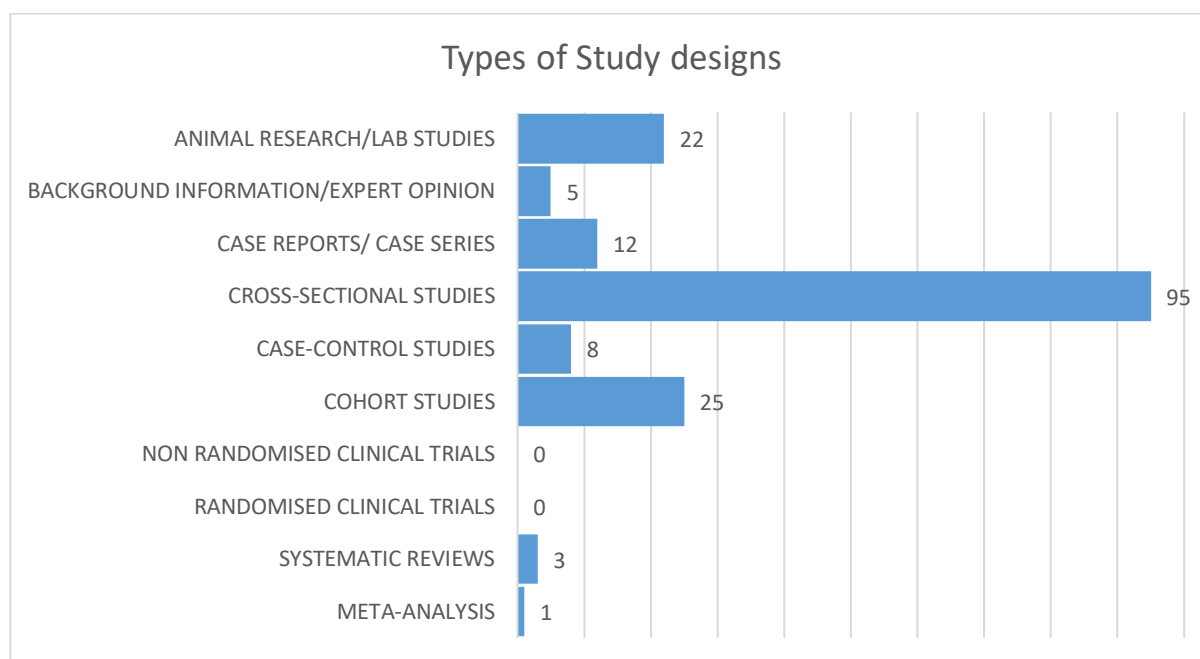

Figure 2: Types of study designs on prostate cancer in Nigeria

Based on Levels of Evidence, most studies (66%), were at level 4a of evidence (figure 3). These include case reports, case series, and cross-sectional studies. Seventeen percent of studies were at the level 5a

evidence levels, including laboratory studies and expert opinion. Nine percent of the studies were at level 2b of evidence, which included cohort studies, 5% at level 3b of evidence including case- control

studies, whilst levels 2c and 2a constituted 2% and 1% respectively. There were no studies at level 1 (a, b or c) of evidence (systematic reviews with homogeneity of randomised clinical trials, individual randomised clinical trials and all or none studies).

Levels of Evidence on Prostate Cancer
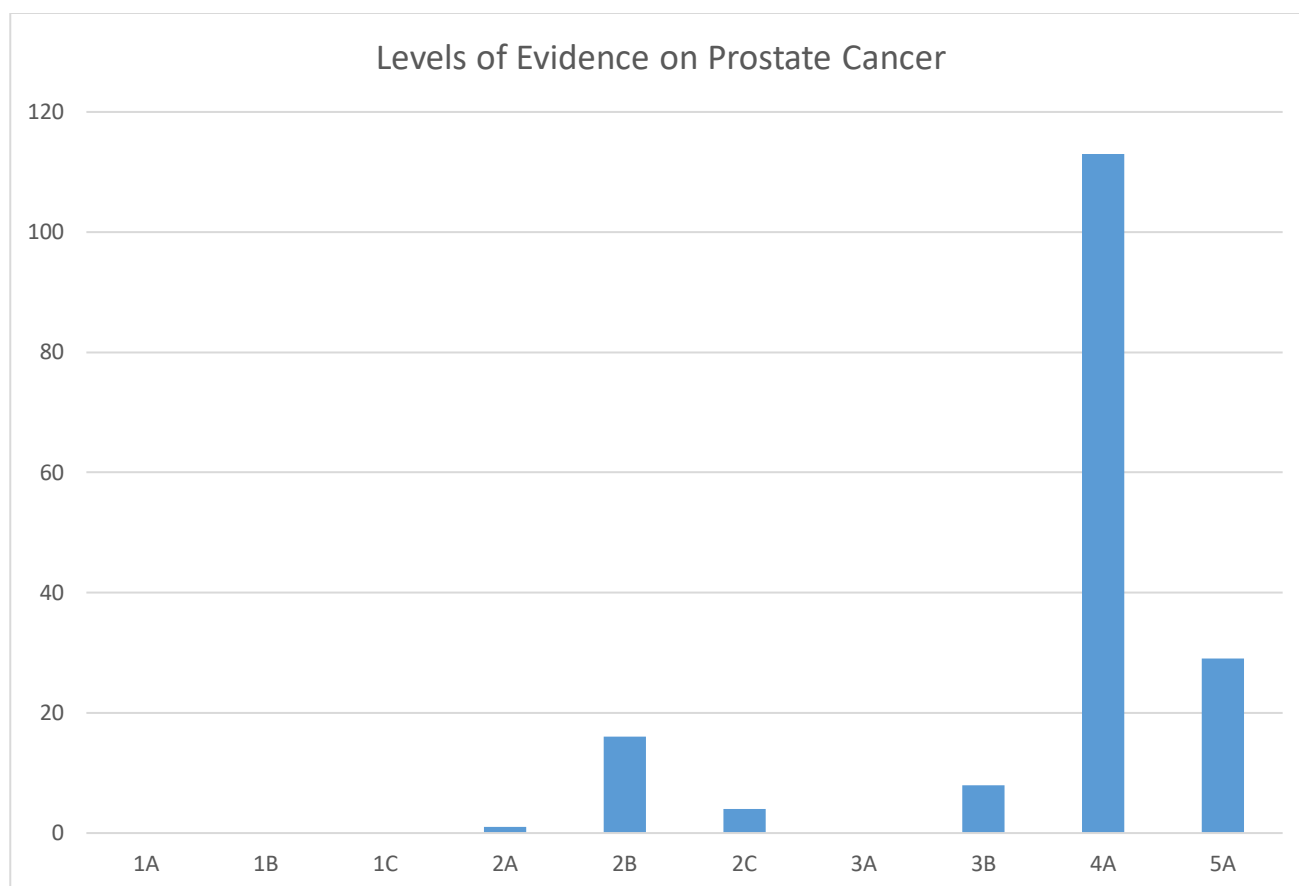
Figure 3: Levels of evidence on prostate cancer research in Nigeria

Most studies were published in 2017 (29 publications were identified that year), followed by 2012, 18 publications, 2013, 2014 and 2015 had 11, 12 & 13 publications respectively (figure 4).
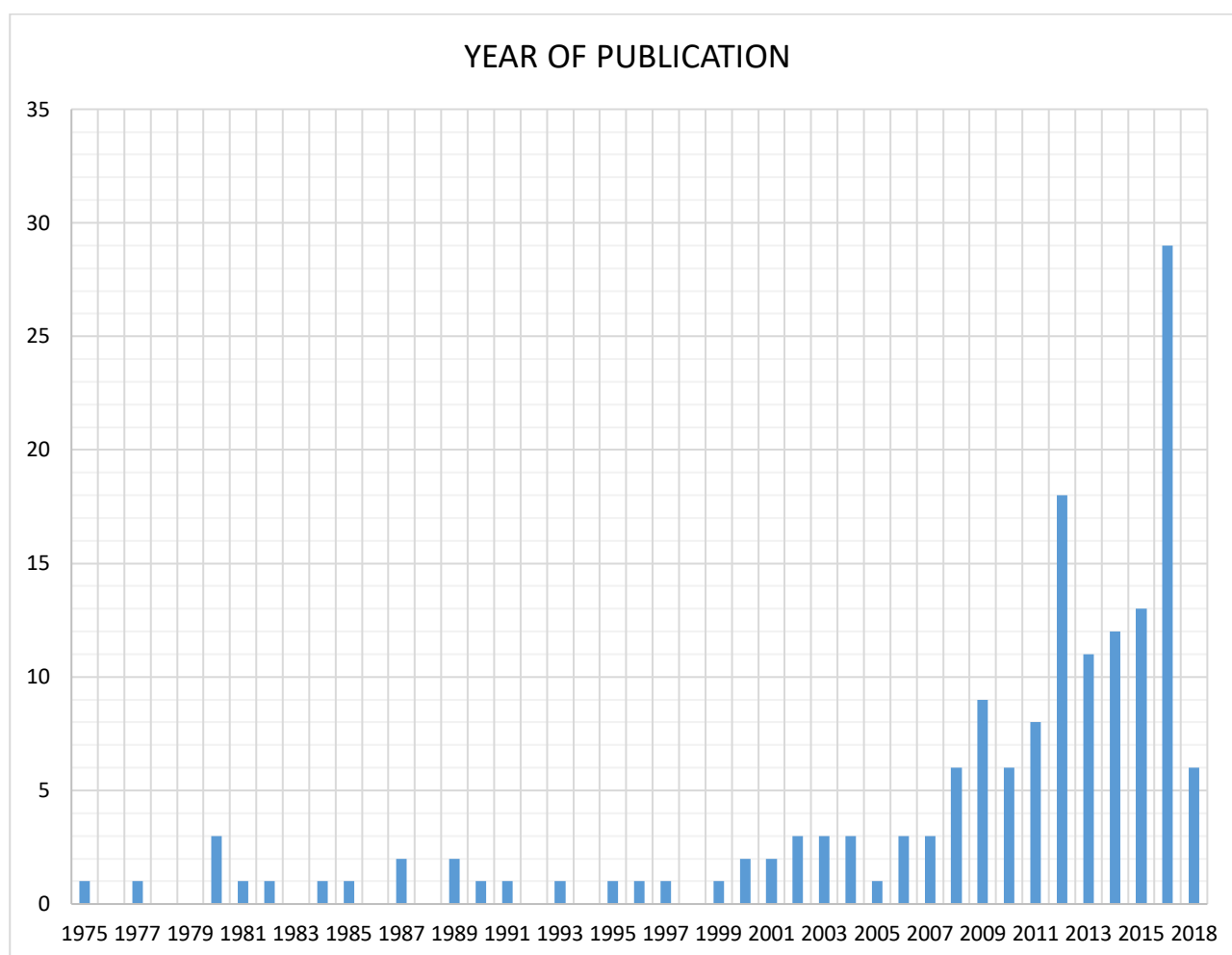
Figure 4: Showing number of publications per year

DISCUSSION

This study demonstrates the paucity of high level evidence research in prostate cancer in Nigeria. It showed that the commonest study design in prostate cancer research conducted in Nigeria is the cross-sectional study. Although, this design can rapidly generate data on some health-related events, it may however be plagued with different types of bias (Sedgwick 2014). Cross sectional studies can be used to generate a hypothesis and establish an association but not causation. Most researchers in Nigeria adopt this methodology because cross sectional studies are relatively cheap and easy to conduct, especially in a low-resource environment where the financial and personnel costs are lower than that required for higher level and more informative studies. There are very limited funding avenues available for research in Nigeria. Studies at higher levels of evidence, like clinical trials, are more rigorous, require higher levels of expertise and are capital intensive. However the benefits of this type of study remain numerous, including their ability to establish causation, assess impact of an intervention and develop treatment guidelines to improve treatment outcomes and survival. (Christensen et al. 2007)

In Nigeria, there are limited efforts to foster high level biomedical research. These efforts are often led by established consortia focused on specific research goals. For example, the Prostate Cancer Transatlantic Consortium (CaPTC), established in 2005, has supported prostate cancer research in Nigeria since 2006 (https://epi.grants.cancer.gov/captc/) . CaPTC is a National Cancer Institute (NCI) Epidemiology and Genomics Research Program (EGRP) supported consortium. CaPTC has over 150 members who are prostate scientists, clinicians, and consumer advocates from countries connected by the Transatlantic Slave Trade, including North America, Europe, the Caribbean, and Africa countries. CaPTC investigators collaborate on projects based on the following scientific aims:

1. Explore and quantify the magnitude of prostate cancer morbidity and mortality variance among Black men of African ancestry;

2. Explore genetic, environmental and behavioral etiology of this variance; and

3. Develop community-sensitive initiatives to control prostate cancer globally.

The official scientific conference for the CaPTC is the *Biennial Science of Global Prostate Cancer Conference for Black men*, which was held in Jacksonville (USA) in 2010, Nassau (Bahamas) in 2012, Montego Bay (Jamaica) in 2014, Orlando (USA) in 2016, and will be held in Ilorin (Nigeria) in 2018. Other active consortia in Nigeria are the African colorectal cancer Group (ARGO), The Men of African Descent and Carcinoma of the Prostate (MADCaP), and Breast Cancer Consortium.

The commonest level of evidence of prostate cancer in this review is level 4, which includes: the case reports, case series, and cross-sectional studies. These levels of evidence are relatively low and are less likely to be adopted in developing treatment guidelines. Most international treatment guidelines are developed based on level 1 evidence, clinical trials. They analyse results from these clinical trials conducted on prostate cancer patients in their countries and then adapt them in the development of treatment guidelines. An example is the STAMPEDE trial in the UK (James et al. 2015) which has led to changes in the standard of care of prostate cancer patients in the UK Another is the CHATTERED trial (Sweeney et al. 2015), a similar clinical trial as the STAMPEDE, which was conducted in the USA. Clinical trials have always sharpened the paradigms of treatment internationally.

The study showed a steep increase in publications on prostate cancer in Nigeria from the year 2000 to date. Despite this increase the proportion remains very low when compared to prostate cancer studies in other countries. The highest number of publications was published in 2017, when a total of 29 articles were published on prostate cancer. When compared with other parts of the world, the USA and UK uniquely had over 300 publications on prostate cancer on PubMed search engine in 2017.

A major reason for low levels of prostate cancer research in Nigeria is the low funding available for cancer research from public and private agencies/organizations. A major funding channel for research in Nigeria is the Tertiary Education Trust Fund (TETFund) established under the TETFund Act (Tertiary Education Trust Fund) in 2011. TETFund gets the funding by imposing a 2% education tax on all registered companies in Nigeria. The fund is disbursed to tertiary educational institutions at Federal and State levels as research grants in all fields (TETFund 2014).

However, the rising trend of cancers in Nigeria necessitates an increase in cancer research funding as exemplified by developed countries. Developed countries have several funding channels for research. These include Government funding and, Non-governmental organisations and charities. In the United States, the 2017 Budget allocated $33.1 billion (0.8%), out of the $4.2 trillion to the National Institute of Health to accelerate ground-breaking research on cancer, precision medicine and others (Sargent et al. 2017). In the UK, the total investment is £26.3 billion between 2016/17 to 2020/21 with an average of £5 billion pounds yearly as allocations for the science and research in the budget (HM Government 2016). It is therefore not surprising that prostate cancer survival has improved in both United States and UK. To make significant leap in fighting prostate cancer in Nigeria, there needs to be focus on funding prostate cancer research. While it will greatly help to have governmental funding, corporate and philanthropic giving will also be very important. In September 2005, the Foundation for Carcinoma of the Prostate Transatlantic Research was established to accelerate prostate cancer research in Nigeria. This foundation is a step in the right way to raise the profile of prostate cancer research in Nigeria.

CONCLUSION

Prostate cancer research is currently at low levels of evidence in Nigeria. As stated by Prof. Folakemi Odedina, "*Actionable research is key to defeating prostate cancer*" (Nigerian Guardian, July 8, 2017). Prostate cancer researchers should make efforts to conduct and publish more studies especially at higher levels of proof like RCTs and metanalysis/systematic reviews of RCT as well as develop treatment guidelines for patients based

on these higher levels of evidence. It is also pertinent that the Nigerian Government increases its efforts in providing the support needed on funding cancer-related research. The Nigerian Government should also develop and implement policies related to increasing cancer research funding through governmental grants. Finally, there needs to be increase in corporate funding and philanthropic funding for prostate cancer research.

Acknowledgements

Conflict of interest

The authors declare that no competing or conflict of interests exists. The funders had no role in study design, writing of the manuscript, or decision to publish.

Authors' contributions

O.A.F, A.C.S & F.B did the manuscript writing and design. O.I, O.O, A.A did the data extraction and literature search. F.C, N.D, F.O supervised the project.

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