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Complete List of Authors:	Morhason-Bello, Imran; University of Ibadan College of Medicine, Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences ; University of Ibadan College of Medicine, Institute of Advanced Medical Research and Training (IAMRAT) Adebamowo, Clement; Center for Bioethics and Research; University of Maryland School of Medicine, Department of Epidemiology and Public Health; Greenebaum Comprehensive Cancer Center and Institute of Human Virology
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Scoping review of the epidemiology of Uterine Fibroid in Black African women

Imran O. Morhason-Bello[1,2] Clement A. Adebamowo[3-4]

[1]Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria
[2]Institute of Advanced Medical Research and Training, College of Medicine, University of Ibadan, Nigeria
[3]Center for Bioethics and Research, Ibadan, Nigeria
[4]Department of Epidemiology and Public Health; and Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Baltimore, MD and Institute of Human Virology, University of Maryland, School of Medicine, Baltimore, MD

Corresponding author:
Clement Adebamowo MD, ScD; Institute of Human Virology Building; University of Maryland, School of Medicine, 725 West Lombard Street, Baltimore, MD 21201
cadebamowo@som.umaryland.edu

Abstract

Objective: Studies, mainly from high-income countries, suggest that there are ethnic and racial variations in prevalence of uterine fibroids (UF). However, there have been few studies of the epidemiology of UF in Sub-Saharan Africa (SSA). We reviewed published articles on the epidemiology of UF in SSA.

Design: This was a scoping review of literature.

Settings: We searched three databases (PubMed, African Wide Information (EBSCO) and African Journals OnLine (AJOL)). The search for eligible articles was conducted between December 2019 and January 2021.

Primary and secondary outcome measures: To describe the reported prevalence/incidence of, and risk factors for UF in SSA.

Results: Of the 1,052 articles retrieved, 9 met the inclusion criteria for review. The articles were from Nigeria (4/9), Ghana (2/9), Cameroon (1/9), Kenya (1/9), and South Africa (1/9). Two studies from pathology departments and three studies from radiology departments reported prevalence of UF. We did not find any study on the incidence or genomics of UF in SSA. Of the three studies that reported on the risk factors of UF, only one case-control study that was conducted using retrospective data of attendees at a gynaecological clinic conducted multivariable analysis.

Conclusion: There is lack of robust epidemiological studies of the prevalence, incidence, and risk factors of UF in SSA. There is urgent need to study epidemiological and genomics risk factors of UF in SSA because UF is the commonest gynaecological neoplasm in this population where it is associated with significant morbidity and occasional, usually perioperative, mortality.

Keywords: *Uterine fibroids, Leiomyoma, Scoping review, epidemiology, Sub-Saharan Africa (SSA)*

Strengths and Limitations

- We comprehensively reviewed all publications on Uterine Fibroids (UF), the commonest neoplasm in African women and found a dearth of robust epidemiological studies and no genomic study on UF in sub-Saharan African women to date (SSA).
- None of the studies we reviewed were sufficiently robust or powered to provide generalizable information on the incidence, prevalence, or risk factors of UF in SSA.
- We identified several research gaps in the epidemiology of UF in SSA.
- This scoping review calls attention to severe and urgent need for research into UF which will enable discovery of actionable risk factors and inform development of novel preventive and therapeutic interventions.
- While unlikely, this review may have omitted eligible articles that are not indexed in any of the three major research databases we searched (PubMed, AWI and AJOL)

Introduction

Uterine fibroids or uterine leiomyomas (UF) are the commonest neoplasms affecting women.[1] They are typically composed of disordered fascicles of smooth muscle cells, vascular smooth-muscle cells, fibroblasts, leiomyoma-associated fibroblasts, and an excess of acellular extracellular matrix (ECM)[2]. They tend to be multiple and may be found in any part of the uterus however, they are commonest in the muscular wall of the uterus (the myometrium).

The incidence and prevalence of UF reported in the literature varies significantly by study design, methods of diagnosis, ethnic composition and age distribution of study participants.[1,3] The cumulative incidence of UFs by the age of 50 years in women in developed countries is 70 – 80%.[1,4]

Variations in the incidence and prevalence of UF by race and ethnic groups have been widely reported. Studies show that the incidence and prevalence of UF in women of African ancestry is higher than that in other races.[4-6] For example, a large longitudinal study (Nurses' Health Study II) in the USA showed that the incidence of UF confirmed by pelvic examination, ultrasound (USS) or hysterectomy per 1000 woman-years was 37.9 in African American, 14.5 in Hispanic, 12.5 in White and 10.4 in Asian women.[5] In another longitudinal study conducted in United Kingdom, the crude incidence of UF based on primary care physicians' diagnosis with USS, hysteroscopy, laparoscopy or pelvic examination was 5.8 per 1000 woman-years.[7]

There are several epidemiological risk factors for UF. These include advanced age, race, age at menarche, low or nulliparity, family history, obesity, diet, physical activity, smoking, oral contraceptives, hormone replacement therapy, environmental exposure to high levels of estrogen and progesterone, and vitamin D deficiency.[3,8-10] Age is consistently associated with the incidence and prevalence of UF irrespective of ethnicity, race and other risk factors. In general, the risk of UF is about 4-11 times higher in women aged 40-60 years compared to 20-30 years old women and women older than 60 years.[1,3] Several studies show that early age at

menarche is associated with higher risk UF.[3,11,12] Multiparity is linearly associated with reduced risk of UF.[3,13] The risk reduction among multiparous women ranges from 20 to 50% compared to nulliparous women.[1]

Overweight and obesity are independent risk factors for UF.[14] A meta-analysis of 325,899 women among whom 19,593 had UF showed association with obesity.[14] The association was present whether obesity was assessed using waist-to-hip ratio (WHR), waist circumference, weight change from age 18 years, or body mass index (BMI).[14] Some studies found a dose response relationship between obesity and UF while other studies did not find such relationship.[3,14-16]

While few studies reported no associations between dietary intakes and UF, other studies showed a reduced risk with consumption of vegetables and fruits, and increased risk with intakes of food additives, sweeteners, soya milk and dietary fats.[1,14,17-19] Most studies found low level of serum vitamin D to be associated with increased risk of UF while a few reported no effect.[20,21] The association between vitamin D and UF was stronger in black compared to White women. Exposure to sunlight for more than an hour a day was also associated with reduced risk of UF.[20] Smoking was associated with reduced risk of UF, especially in women with low BMI.[1] Most studies reported an inverse relationship between regular physical activities and risk of UF.[3,19] Oral and injectable contraceptives use were associated with reduced risk of UF, however a few studies found increased or no risk in women using oral contraceptives.[1,3] Hormone replacement therapy or exposure to exogenous hormones, particularly among postmenopausal women was associated with increased risk of UF in some studies.[3]

Genetic and epigenetic factors have been associated with risk of UF. Positive family history is associated with increased risk of UF and higher risk was reported among sisters.[1,22-26] The estimates of heritability for UF were 26 to 69% in twin studies while data from GWAS reported

heritability risk of 13%.[27,28] The risk of UF is 2.5-fold among first degree relatives compared with the general population.[28] The concordance rate of UF among monozygotic twins is twice that of dizygotic twins of the same sex, and a lot higher than in first-degree relatives.[28,29] Recently, genome wide association studies (GWAS) identified several candidate loci for UF in chromosome regions among African American - 22q13.1 (*CYTH4*), Caucasian - 11p15.5 (*BETIL*), 17q25.3 (*FASN, CCDC57, and SLC16A3*), 22q13.1 (*TNRC6B*), and Asian - 10q24.33 (*OBFC1*), 11p15.5(*BET1L*), and 22q13.1 (*TNRC6B*) – populations.[30-33]

UF is associated with significant morbidity and substantial socio-economic costs.[34-36] Data from a global systematic review of the cost of UF showed that the total direct and indirect cost after diagnosis or from surgical care ranged from US$11,717 to 25,023 per patient per year.[37] In United States, the annual cost of UF to the economy was estimated to be between US$5.9 to 34.4 billion with obstetric complications contributing the highest fraction of the economic burden.[38]

Consistent with the high incidence and prevalence of UF in African populations in developed countries, case reports and clinical evidence suggest high prevalence of UF in black women living in Africa. However, in contrast to developed countries, there have been very few, adequately powered, systematic epidemiological studies of UF in Africa. In this scoping review of current publications on the epidemiology of UF in Africa, we aim to establish the state of the evidence and their limitations, the burden of UF and priorities for research on UF in black women living in SSA.

Methods

In this review, we used the Joanna Briggs Institute (JBI) guidelines for the conduct of systematic scoping review which was earlier described by Arksey and O'Malley.[39,40] Briefly, we base this review on five frameworks: (a) identifying the research question, (b) identifying the relevant studies (search strategy), (c) selecting the eligible studies, (d) charting the data and (e) collating, summarising, and reporting the results with or without consultation with experts on the specific field. [40]

Research question

The research questions for this scoping review are: What are the prevalence and incidence of UF among black women in SSA? What are the risk factors for UF among SSA women?

Information sources and search strategy

We conducted a systematic search of three online databases for records in English: PubMed, African Wide Information (EBSCO) and African Journal Online (AJOL). We used the following keywords to search the databases to retrieve published articles on the incidence, prevalence, and risk factors of UF; uterine fibroids or fibroids or leiomyoma or myoma; prevalence, incidence, risk factors or causes and Sub-Saharan Africa (SSA) (using sub-regions within SSA (West Africa OR East Africa OR Central Africa OR Southern Africa), and by specific country names). We used Boolean terms AND/OR to separate the keywords during the search. We included Medical Subject Headings (MeSH) terms in the search terms. We also manually searched references and bibliography of relevant articles on this subject. The search was conducted between December 2019 and 27th January 2021.

Eligibility criteria

We used the PICO format (population, intervention, comparator, and outcome) to design the eligibility criteria for the studies that were included in this review. These are (a) published peer reviewed article with observational or experimental design that reported on the aetiology or

risk factors or incidence or prevalence or proportion of women with UFs and (b) data must have been collected in SSA among indigenous black women population. We excluded case reports, letter to editors or expert opinion without primary data on UFs in SSA as well as studies that only reported the outcome of treatment.

Study Selection process

All titles retrieved from searches were compiled and reviewed with Endnote X 8.0 (Thompson Reuters). We removed all duplicates using the Endnote automated system and manually. We screened abstracts in accordance with our inclusion and exclusion criteria. Next, we screened the full texts of abstracts that were eligible for further consideration. Only articles that met the inclusion criteria during full text screening were finally selected for data charting in this review.

Charting data

We entered our data into a prepared Microsoft Excel sheet using the following data charting fields: authors, date, country, study design, aim/objectives, sample size, recruitment strategy (probability or non-probability sampling), study settings (health facility/community/online), outcome measured (prevalence/incidence/proportion), analysis (descriptive/test of association/multivariable analysis) and summary of key findings.

Collating, summarising, and reporting the results

We present a descriptive summary of eligible studies and we created a Prisma-ScR flow chart to summarise the process and number of articles that were finally selected for data charting.[41] The chart shows the overall number of studies included, study designs and settings, publication years, the characteristics of the study populations, the outcomes reported, and the countries where the studies were conducted. In line with scoping reviews' methodology, we did not perform an assessment of the quality of the included studies.

Patient and Public Involvement

It was not possible to describe patient and public involvement in this research.

Results

We retrieved 1,052 studies from the three databases (Figure 1). After removal of duplicate publications, we screened 484 titles and abstracts and found only 48 articles were eligible for full-text screening. We excluded 39 of the 48 full text articles because 17 of them were on symptoms/management of UF, 7 were animal studies, 5 each were case reports and reviews, 2 were from outside SSA, 1 each were on recurrent UF after treatment, full texts not available and on somatic genetic mutation in UF. Of the 9 studies that met the inclusion criteria, 4 were from Nigeria,[42-45] 2 from Ghana,[46,47] and 1 study each from Cameroon,[48] Kenya[49] and South Africa.[50]

Incidence or prevalence of UF

Five of the 9 studies screened described the prevalence of UF (Table 1).[42,44,46,48,50] Two of these studies, one each from pathology departments in single institutions in South Africa and Nigeria, examined the proportion of UF in surgical specimens.[42,50] In Northern Nigeria, UF accounted for 2.2% of all surgical specimen at a single facility over a five-year period.[42] The South African study reported that the proportion of UF among all hysterectomy specimens in a single institution over a six-month period was 64.6%.[50]

A cross-sectional study of pregnant women undergoing abdominal USS examination in two regional hospitals in Cameroun reported that 16.8% (38/226) had UF.[48] Another cross-sectional study in Ghana among 244 non-pregnant women referred for abdominal USS showed that 36.9% had UF and the proportion of women with UF increased with age.[46] A 2-year retrospective review of attendees at the gynaecology clinic of a public tertiary health institution in Nigeria showed that 30.7% (178/580) of all patients had a diagnosis of UF.[44] Another study of pregnant women referred for prenatal abdominal USS at a tertiary hospital in eastern Nigeria showed that the prevalence of UF was 12.3% during pregnancy.[43]

Role of Oestrogen, Progesterone, and their receptors

A study in Kenya reported on cytosolic quantification of oestrogen and progesterone and their receptors in UF tissue measured using radioimmunoassay.[49] The study showed that UF contained lower levels of oestrogen and progesterone but higher levels of receptors for these hormones compared to normal uterine tissue.[49] In a more recent Nigerian study using immunohistochemistry, the level of oestrogen and progesterone receptors in UF was higher than in uterine tissue.[45] The Nigerian study further showed a significant negative correlation between UF size and the progesterone receptors levels only (Table 1).[45]

Risk factors for UF

Three studies presented data on risk factors of UF (Tables 1 and 2).[44,46,48] In a Nigerian case-control study of gynaecology clinic attendees, advanced age (OR=4.90; 95%CI 1.80-31.1) and positive family history (OR=3.0; 95%CI 1.90-4.80) were associated with higher risk while obesity (OR=0.4; 95%CI 0.10-0.90) and primiparity (OR=0.60; 95%CI 0.20-0.90) were associated with lower risk of UF.[44] A cross-sectional study of 244 women referred for abdominal USS at three centres in Ghana found that women with UF tended to be older (p=0.001), obese (0.001), older at last pregnancy and delivery (p=0.001) and have lower parity (p=0.001). [46] In another cross-sectional study of factors associated with UF in pregnancy in Cameroun, women with UF were older (p<0.001) and had higher gravidity (p=0.02). [48]

Discussion

In this review, we mapped published epidemiological studies on incidence, prevalence, and risk factors for UF in indigenous African women. Our results confirmed the paucity of systematic epidemiological study of UF among black women in Africa. Only few studies have some information on prevalence/proportion of, and risk factors for UF.[42,44,46,48,50] The five studies that reported the prevalence of UF used different populations, denominators, and study designs.[42,44,46,48,50] Two studies from pathology departments in Nigeria and South Africa used different reporting periods and denominators to calculate the proportions of UF.[42,50] We also observed variations in the reporting of the prevalence of UF in pregnancy in the two studies from radiology departments in Nigeria and Cameroon.[43,48] They both used convenience sampling technique and were silent on the gestational ages of participants. The only Nigerian study that presented data on the prevalence of UF among non-pregnant women was a retrospective review of case records that used all other attendees at a gynaecological clinic as controls.[44] There was no study in this review that has information on the incidence of UF in pregnant or non-pregnant women.

Two studies were on the role of oestrogen and progesterone and their receptors. The two hormonal studies used different diagnostic techniques (radioimmunoassay versus immunochemistry), laboratory estimation of cut-off levels for oestrogen and progesterone and comparator groups (UF and normal myometrial tissue from same patient versus UF and normal myometrial tissue from different patients as cases and control).[45,49] The observed differences in the methodology of the two studies make it difficult to compare and interpret their findings. We observed that the sample sizes of these three studies were too small to allow for rigorous multivariable analysis for confounders. In addition, the three studies were conducted with specimen from women who had treatment in specific health facilities.

Three studies described risk factors for UF among black African women, but they all used different research designs and data analysis techniques.[44,46,48] All the studies were conducted within single facilities, two were cross-sectional and one was a retrospective case control study. The risk factors identified in the three studies were similar to those reported in studies conducted in USA, Europe and Asia. [5,12,51] Briefly, advancing age was the only risk factors that was common to all three studies and low parity was reported in two studies.[44,46,48] The only other risk factor reported among non-pregnant women was self-report of family history of UF.[44] Obesity was reported as a protective factor in non-pregnant Nigerian women and as a risk factor in pregnant women in Ghana.[44,48] The tests for association in these studies were not well described in the methods sections of their manuscripts.[44,46,48] The studies from Cameroon and Ghana used bivariate tests and did not adjust for age in their analyses.[46,48] The only Nigerian study that used multivariable analysis to adjust for confounders, used data collected from a retrospective review of cases managed in a tertiary public health facility and assigned other attendees as controls.[44]

Although, we did not assess the risk of bias in studies that we reviewed because that is outside the objective of scoping review generally, we observed that the majority of the studies used data collected from case series or cross-sectional studies (6/9) while two (3/9) were case control studies.[42-50] None of the 9 studies we reviewed used probability sampling technique to select their subjects and only one study reported on sample size and power calculation.

We found several gaps in the epidemiology of UF in SSA. There was no genomic epidemiology study of uterine fibroid in SSA. Studies from high income countries have shown that only 20.0-40.0% of women with symptomatic UF seek medical treatment, suggesting that a significant number of women with UF are not captured by facilities based studies.[52] We did not find any published population based study with adequate statistical power and sampling strategy which can generate generalizable information on incidence, prevalence and risk factors of UF among

indigenous black African women. There are many epidemiological risk factors of UF that are yet to be investigated in SSA. These factors include reproductive factors (age at menarche and menopause, birth interval or inter pregnancy interval, contraceptives, and hormone replacement therapy), diets including vitamin D, trace elements and heavy metals, lifestyle and physical activity, reproductive tract infections, microbiome, and pollution. [3,8,12,53,54] Lack of information on these risk factors prevent development of preventive and therapeutic interventions. This is a serious gap in knowledge considering the morbidity, mortality, and economic costs of UF in SSA.

The interpretation of findings from this scoping review may be limited for the following reasons. We searched published articles from online databases only. We may have missed papers published in journals that are not indexed in these online databases. We excluded one article that we could not retrieve the full texts, but the abstract shows that this was on the association between UF and BMI. Despite these limitations, this scoping review confirmed the dearth of studies on the epidemiology of UF among SSA women and argues for urgent remediation of this situation.

Conclusions

Our results show that there is limited information on the epidemiology of UF and identified gaps in knowledge of UF among women in SSA despite its high prevalence, morbidity, and economic costs. We recommend urgent implementation of well-designed and adequately powered studies to address this gap.

Authors' contribution: CAA conceived and designed the study. He conducted literature review, reviewed, revised, and approved the manuscript. IMB participated in the design, conducted literature search, screening of articles and data charting. He wrote the first draft, revised, and approved the manuscript.

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Patient consent for publication: Not required.

Ethical Approval: Ethical approval is not required for the scoping review.

Data availability statement: The data will be made available upon request from the corresponding author.

References:

1. Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. *BJOG* 2017; **124**(10): 1501-12.

2. Holdsworth-Carson SJ, Zaitseva M, Vollenhoven BJ, Rogers PA. Clonality of smooth muscle and fibroblast cell populations isolated from human fibroid and myometrial tissues. *Molecular human reproduction* 2014; **20**(3): 250-9.

3. Wise LA, Laughlin-Tommaso SK. Epidemiology of Uterine Fibroids: From Menarche to Menopause. *Clin Obstet Gynecol* 2016; **59**(1): 2-24.

4. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol* 2003; **188**(1): 100-7.

5. Marshall LM, Spiegelman D, Barbieri RL, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstet Gynecol* 1997; **90**(6): 967-73.

6. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Age-specific incidence rates for self-reported uterine leiomyomata in the Black Women's Health Study. *Obstet Gynecol* 2005; **105**(3): 563-8.

7. Martin-Merino E, Wallander MA, Andersson S, Soriano-Gabarro M, Rodriguez LA. The reporting and diagnosis of uterine fibroids in the UK: an observational study. *BMC Womens Health* 2016; **16**: 45.

8. Brakta S, Diamond JS, Al-Hendy A, Diamond MP, Halder SK. Role of vitamin D in uterine fibroid biology. *Fertil Steril* 2015; **104**(3): 698-706.

9. Baird DD, Harmon QE, Upson K, et al. A Prospective, Ultrasound-Based Study to Evaluate Risk Factors for Uterine Fibroid Incidence and Growth: Methods and Results of Recruitment. *Journal of women's health* 2015; **24**(11): 907-15.

10. Wise LA, Palmer JR, Rosenberg L, Haddad SA, Ruiz-Narvaez EA. FASN, dietary fat intake, and risk of uterine leiomyomata in the Black Women's Health Study. *Fertil Steril* 2016; **106**(5): 1136-41.

11. Styer AK, Rueda BR. The Epidemiology and Genetics of Uterine Leiomyoma. *Best practice & research Clinical obstetrics & gynaecology* 2016; **34**: 3-12.

12. Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. *Int J Fertil Steril* 2016; **9**(4): 424-35.

13. Baird DD, Dunson DB. Why is parity protective for uterine fibroids? *Epidemiology* 2003; **14**(2): 247-50.

14. Qin H, Lin Z, Vásquez E, Luan X, Guo F, Xu L. Association between obesity and the risk of uterine fibroids: a systematic review and meta-analysis. *J Epidemiol Community Health* 2021; **75**(2): 197-204.

15. Lee JE, Song S, Cho E, et al. Weight change and risk of uterine leiomyomas: Korea Nurses' Health Study. *Curr Med Res Opin* 2018; **34**(11): 1913-9.

16. Sato F, Nishi M, Kudo R, Miyake H. Body fat distribution and uterine leiomyomas. *J Epidemiol* 1998; **8**(3): 176-80.

17. Shen Y, Xu Q, Xu J, Ren ML, Cai YL. Environmental exposure and risk of uterine leiomyoma: an epidemiologic survey. *Eur Rev Med Pharmacol Sci* 2013; **17**(23): 3249-56.

18. Wise LA, Radin RG, Kumanyika SK, Ruiz-Narvaez EA, Palmer JR, Rosenberg L. Prospective study of dietary fat and risk of uterine leiomyomata. *Am J Clin Nutr* 2014; **99**(5): 1105-16.

19. He Y, Zeng Q, Dong S, Qin L, Li G, Wang P. Associations between uterine fibroids and lifestyles including diet, physical activity and stress: a case-control study in China. *Asia Pac J Clin Nutr* 2013; **22**(1): 109-17.

20. Baird DD, Hill MC, Schectman JM, Hollis BW. Vitamin d and the risk of uterine fibroids. *Epidemiology* 2013; **24**(3): 447-53.

21. Ciebiera M, Włodarczyk M, Ciebiera M, Zaręba K, Łukaszuk K, Jakiel G. Vitamin D and uterine fibroids—review of the literature and novel concepts. *International journal of molecular sciences* 2018; **19**(7): 2051.

22. D'Aloisio AA, Baird DD, DeRoo LA, Sandler DP. Early-life exposures and early-onset uterine leiomyomata in black women in the Sister Study. *Environ Health Perspect* 2012; **120**(3): 406-12.

23. Mu X, Du X, Yao K, et al. Association between HSD17B1 rs605059 polymorphisms and the risk of uterine diseases: a systemic review and meta-analysis. *International journal of clinical and experimental pathology* 2015; **8**(6): 6012-8.

24. Bideau VS, Alleyne AT. Leu/Val SNP polymorphism of CYP1B1 and risk of uterine leiomyoma in a Black population. *Tumour Biol* 2016; **37**(3): 4035-40.

25. Gallagher CS, Morton CC. Genetic Association Studies in Uterine Fibroids: Risk Alleles Presage the Path to Personalized Therapies. *Seminars in reproductive medicine* 2016; **34**(4): 235-41.

26. Aissani B, Zhang K, Wiener H. Genetic determinants of uterine fibroid size in the multiethnic NIEHS uterine fibroid study. *Int J Mol Epidemiol Genet* 2015; **6**(1): 9-19.

27. Ponomarenko I, Reshetnikov E, Polonikov A, et al. Candidate Genes for Age at Menarche Are Associated With Uterine Leiomyoma. *Front Genet* 2020; **11**: 512940.

28. Luoto R, Kaprio J, Rutanen EM, Taipale P, Perola M, Koskenvuo M. Heritability and risk factors of uterine fibroids--the Finnish Twin Cohort study. *Maturitas* 2000; **37**(1): 15-26.

29. Vikhlyaeva EM, Khodzhaeva ZS, Fantschenko ND. Familial predisposition to uterine leiomyomas. *Int J Gynaecol Obstet* 1995; **51**(2): 127-31.

30. Hellwege JN, Jeff JM, Wise LA, et al. A multi-stage genome-wide association study of uterine fibroids in African Americans. *Hum Genet* 2017; **136**(10): 1363-73.

31. Edwards TL, Michels KA, Hartmann KE, Velez Edwards DR. BET1L and TNRC6B associate with uterine fibroid risk among European Americans. *Hum Genet* 2013; **132**(8): 943-53.

32. Cha P-C, Takahashi A, Hosono N, et al. A genome-wide association study identifies three loci associated with susceptibility to uterine fibroids. *Nature genetics* 2011; **43**(5): 447-50.

33. Eggert SL, Huyck KL, Somasundaram P, et al. Genome-wide linkage and association analyses implicate FASN in predisposition to uterine leiomyomata. *The American Journal of Human Genetics* 2012; **91**(4): 621-8.

34. Agboola AD, Bello OO, Olayemi OO. A clinical audit of the patterns of presentations and complications of abdominal myomectomy at the University College Hospital, Ibadan, Nigeria. *J Obstet Gynaecol* 2021: 1-6.

35. Yorgancı A, Meydanlı MM, Kadıoğlu N, et al. Incidence and outcome of occult uterine sarcoma: A multi-centre study of 18604 operations performed for presumed uterine leiomyoma. *J Gynecol Obstet Hum Reprod* 2020; **49**(1): 101631.

36. Foth D, Rohl FW, Friedrich C, et al. Symptoms of uterine myomas: data of an epidemiological study in Germany. *Arch Gynecol Obstet* 2017; **295**(2): 415-26.

37. Soliman AM, Yang H, Du EX, Kelkar SS, Winkel C. The direct and indirect costs of uterine fibroid tumors: a systematic review of the literature between 2000 and 2013. *American journal of obstetrics and gynecology* 2015; **213**(2): 141-60.

38. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol* 2012; **206**(3): 211 e1-9.

39. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis, JBI, 2020. Available from https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-20-12. 2020.

40. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International journal of social research methodology* 2005; **8**(1): 19-32.

41. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of Internal Medicine* 2018; **169**(7): 467-73.

42. Mohammed A, Shehu S, Ahmed S, et al. Uterine leiomyomata: a five year clinicopathological review in Zaria, Nigeria. *Nigerian Journal of surgical research* 2005; **7**(1): 206-8.

43. Eze CU, Odumeru E, Ochie K, Nwadike U, Agwuna K. Sonographic assessment of pregnancy co-existing with uterine leiomyoma in Owerri, Nigeria. *African Health Sciences* 2013; **13**(2): 453-60.

44. Oluwole A, Owie E, Babah O, Afolabi B, Oye-Adeniran B. Epidemiology of Uterine Leiomyomata at the Lagos University Teaching Hospital, Idi-Araba, Lagos. *Nigerian Hospital Practice* 2015; **15**(1-3): 14-20.

45. Awowole IO, Makinde ON, Badejoko OO, et al. Clinical correlates of leiomyoma estrogen and progesterone receptors among Nigerian women. *International Journal of Gynecology & Obstetrics* 2016; **135**(3): 314-8.

46. Sarkodie BD, Botwe BO, Adjei DN, Ofori E. Factors associated with uterine fibroid in Ghanaian women undergoing pelvic scans with suspected uterine fibroid. *Fertility research and practice* 2016a; **2**(1): 1-7.

47. Sarkodie BD, Botwe BO, Ofori EK. Uterine fibroid characteristics and sonographic pattern among Ghanaian females undergoing pelvic ultrasound scan: a study at 3-major centres. *BMC women's health* 2016b; **16**(1): 1-6.

48. Egbe TO, Badjang TG, Tchounzou R, Egbe E-N, Ngowe MN. Uterine fibroids in pregnancy: prevalence, clinical presentation, associated factors and outcomes at the Limbe and Buea Regional Hospitals, Cameroon: a cross-sectional study. *BMC research notes* 2018; **11**(1): 1-6.

49. Wango EO, Tabifor HN, Muchiri LW, Sekadde-Kigondu C, Makawiti DW. Progesterone, estradiol and their receptors in leiomyomata and the adjacent normal myometria of black Kenyan women. *African journal of health sciences* 2002; **9**(2): 123-8.

50. Tiltman AJ. Leiomyomas of the uterine cervix: a study of frequency. *International journal of gynecological pathology: official journal of the International Society of Gynecological Pathologists* 1998; **17**(3): 231-4.

51. Wise LA, Palmer JR, Harlow BL, et al. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African-American women: a prospective study. *Am J Epidemiol* 2004; **159**(2): 113-23.

52. Marsh EE, Ekpo GE, Cardozo ER, Brocks M, Dune T, Cohen LS. Racial differences in fibroid prevalence and ultrasound findings in asymptomatic young women (18-30 years old): a pilot study. *Fertil Steril* 2013; **99**(7): 1951-7.

53. Hansen JG, Tang W, Hootman KC, et al. Genetic and environmental factors are associated with serum 25-hydroxyvitamin D concentrations in older African Americans. *J Nutr* 2015; **145**(4): 799-805.

54. Moore KR, Cole SR, Dittmer DP, Schoenbach VJ, Smith JS, Baird DD. Self-Reported Reproductive Tract Infections and Ultrasound Diagnosed Uterine Fibroids in African-American Women. *Journal of women's health* 2015; **24**(6): 489-95.

Table 1: Descriptive analysis of studies included in the scoping review

Author; Year [Country]	Research focus	Study design	Sampling methods	Sample size	Outcome measured	Age of study participants	Summary of key findings
Tiltman et. al. 1998 [South Africa]	Pathology	Case series	Non-probability	661	Proportion of UF within hysterectomy specimen	12.0-84.0	The proportion of UF was 427/661 (64.6%)
Wango et. al. 2002 [Kenya]	Pathology	Case series	Not clearly described	20	Evaluation of estradiol, progesterone, and their receptors	Range 31.0-42.0	The UF tissue contained significantly higher levels of estrogen receptor (28.2±1.6 vs 19.1±0.4 fm/mg protein) and progesterone receptor (16.8±0.7 vs 9.4±0.2 fm/mg protein) compared to normal myometrial tissue, a relatively significant higher levels of estrogen (1117.6±20.9 vs 616.9±19.8 pm/mg protein) and progesterone (7.7±0.25 vs 3.2±0.34 nm/mg protein) in the myometrium than in the leiomyomata.
Mohammed et. al. 2005 [Nigeria]	Pathology	Case series	Non-probability	209	Proportion of UF pathological specimen & degenerative changes	Range 25.0-50.0	The proportion of myometrial UF was 2.2% of all surgical specimen over five years.
Eze et. al. 2013 [Nigeria]	Radiology	Case control	Non-probability	200 (100 cases vs 100 controls)	Frequency and growth rate of uterine fibroids in pregnancy	Cases (31.6 ± 4.5yr); Controls (29.1 ± 5.5yr)	The frequency of UFs in pregnancy was 12.3%; the commonest type was subserous fibroids (27.5%). The mean size of UFs measured on ultrasound was lowest during third scan.
Oluwole et. al. 2015 [Nigeria]	Clinical	Case control	Non-probability	580	Proportion of UF & risk factor analysis	35.5±5.8	The proportion of women with UFs was 31% (178/580). Presence of UFs was associated with 40-49years (OR=4.9%; 95%CI 1.8-31.1); lower parity (OR=0.6; 95%CI 0.2-0.9); family history of UFs (OR=1.9; 95%CI 1.9-4.8); and history of infertility (OR=5.0; 95%CI 0.9-25.9)
Awowole et. al. 2016 [Nigeria]	Pathology	Cross-sectional	Non-probability	60	To measure expression of estrogen receptor α (ERα) and progesterone receptor (PR) in myometrium and UF	26.0-53.0	UF had a higher mean expression of estrogen receptor (Erα) (H-score 193.4 ± 64.6 vs 153.3 ± 69.1; p = 0.01) and progesterone receptor (PR) (214.9 ± 66.6 vs 171.5 ± 63.5; p < 0.001) than in myometrial tissues. The tumor diameter correlated negatively with the immunoscores of both receptors irrespective of age, parity, and body mass index, but this was only significant for PR (p = –0.44; p<0.001).
Sarkodie et. al. 2016a [Ghana]	Radiology	Cross-sectional	Non-probability	244	Prevalence of UF & risk factors analysis	14.0-54.0	In this study, 23 % (38/168) of women <35 had prevalent fibroids, compared to 67 % (36/54) of women 35–44, and 73 % (16/22) of women at 45 or above years.

							Factors that associated significantly with UF in Ghanaian women included obesity (X2 = 17.3, p-value = 0.001), participant's age range (X2 = 47.4, p = 0.001), parity (X2 = −10.2, p = 0.001), and age at last delivery (X2 = 34.6, p = 0.001).
Sarkodie et. al. 2016b [Ghana]	Radiology	Cross-sectional	Non-probability	244	Assessment of sonographic characteristics of UF	14.0-54.0	The prevalence of UF was 36.9 % (90/244). The majority of the UFs were intramural (57.8 %) with only 4.4 % noted as sub-mucosal. Most (55.6 %) of the UFs were located in more than one part of the uterus.
Egbe et. al. 2018 [Cameroon]	Radiology & Clinical	Cross-sectional	Non-probability	226	Proportion of UF & risk factors analysis	≥21.0	The prevalence of UF in pregnancy was 16.7% (38/226). Respondents with UF were older than those without (p < 0.001) and of low parity (p = 0.02).

UF – Uterine Fibroids; CI – Confidence interval; OR – Odds ratio

Table 2: Summary of reported risk factors associated with UF in SSA

Risk factors	Pregnant women		Non-Pregnant women
	Egbe et. al. 2018 [Cross-sectional study from Cameroon]	**Sarkodie et. al. 2016a [Cross-sectional study from Ghana]**	**Oluwole et. al. 2015 [Case control study from Nigeria]**
Advanced age	↑	↑	↑
Family history	Not considered	Not considered	↑
Obesity	Not considered	↑	↓
Nulliparity	Not considered	↑	Not considered
Gravidity	↑	Not considered	Not considered
Advanced age at delivery	Not considered	↑	Not considered
At least primiparity	Not considered	Not considered	↓

↑ - Increased risk, ↓ - Decreased risk, Not considered as a risk factor in the study

Figure 1: The Prisma Flow Chart for the scoping review

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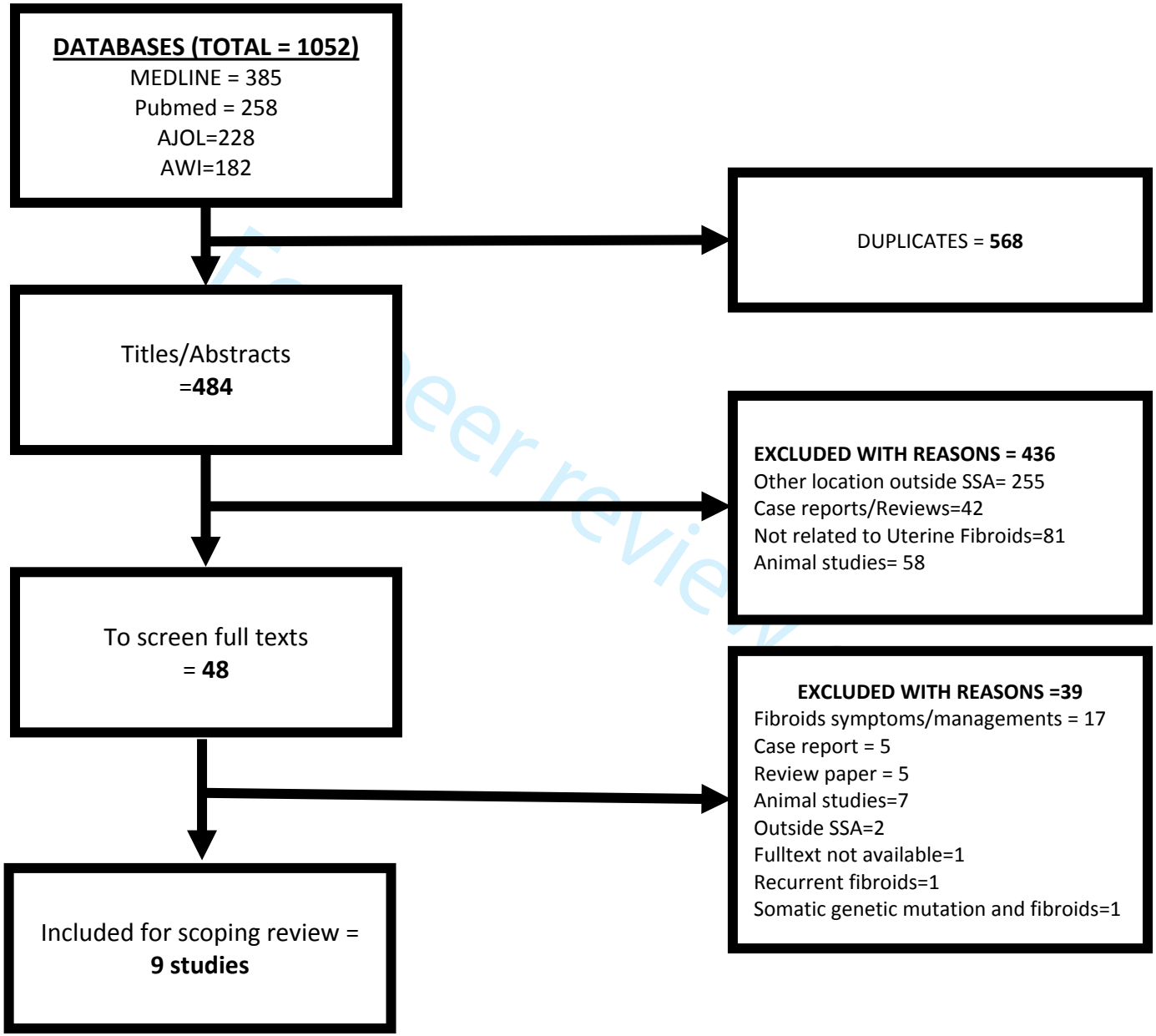

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Systematic review of the epidemiology of Uterine Fibroid in African women

Imran O. Morhason-Bello[1,2] Clement A. Adebamowo[3-4]

[1]Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria
[2]Institute of Advanced Medical Research and Training, College of Medicine, University of Ibadan, Nigeria
[3]Center for Bioethics and Research, Ibadan, Nigeria
[4]Department of Epidemiology and Public Health; and Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Baltimore, MD

Corresponding author:
Clement Adebamowo MD, ScD; Department of Epidemiology and Public Health, University of Maryland, School of Medicine, 600 West Redwood Street, Baltimore, MD 21201
cadebamowo@som.umaryland.edu

Abstract

Objective: Studies, mainly from high-income countries, suggest that there are ethnic and racial variations in prevalence of uterine fibroids (UF). However, there have been few studies of the epidemiology of UF in Sub-Saharan Africa (SSA). We reviewed published articles on the epidemiology of UF in SSA.

Design: This was a scoping review of literature.

Settings: We searched three databases (PubMed, African Wide Information (EBSCO) and African Journals OnLine (AJOL)). The search for eligible articles was conducted between December 2019 and January 2021.

Primary and secondary outcome measures: To describe the reported prevalence/incidence of, and risk factors for UF in SSA.

Results: Of the 1,052 articles retrieved, 9 met the inclusion criteria for review. The articles were from Nigeria (4/9), Ghana (2/9), Cameroon (1/9), Kenya (1/9), and South Africa (1/9). Two studies from pathology departments and three studies from radiology departments reported prevalence of UF. We did not find any study on the incidence or genomics of UF in SSA. Of the three studies that reported on the risk factors of UF, only one case-control study that was conducted using retrospective data of attendees at a gynaecological clinic conducted multivariable analysis.

Conclusion: There is lack of robust epidemiological studies of the prevalence, incidence, and risk factors of UF in SSA. There is urgent need to study epidemiological and genomics risk factors of UF in SSA because UF is the commonest gynaecological neoplasm in this population where it is associated with significant morbidity and occasional, usually perioperative, mortality.

Keywords: *Uterine fibroids, Leiomyoma, Scoping review, epidemiology, Sub-Saharan Africa (SSA)*

Strengths and Limitations

- We comprehensively reviewed all publications on Uterine Fibroids (UF), the commonest neoplasm in African women and found a dearth of robust epidemiological studies and no genomic study on UF in sub-Saharan African women to date (SSA).
- None of the studies we reviewed were sufficiently robust or powered to provide generalizable information on the incidence, prevalence, or risk factors of UF in SSA.
- We identified several research gaps in the epidemiology of UF in SSA.
- This scoping review calls attention to severe and urgent need for research into UF which will enable discovery of actionable risk factors and inform development of novel preventive and therapeutic interventions.
- While unlikely, this review may have omitted eligible articles that are not indexed in any of the three major research databases we searched (PubMed, AWI and AJOL)

Introduction

Uterine fibroids or uterine leiomyomas (UF) are the commonest neoplasms affecting women.[1] They are typically composed of disordered fascicles of smooth muscle cells, vascular smooth-muscle cells, fibroblasts, leiomyoma-associated fibroblasts, and an excess of acellular extracellular matrix (ECM)[2]. They tend to be multiple and may be found in any part of the uterus however, they are commonest in the muscular wall of the uterus (the myometrium).

The incidence and prevalence of UF reported in the literature varies significantly by study design, methods of diagnosis, ethnic composition and age distribution of study participants.[1,3] The cumulative incidence of UFs by the age of 50 years in women in developed countries is 70 – 80%.[1,4]

Variations in the incidence and prevalence of UF by race and ethnic groups have been widely reported. Studies show that the incidence and prevalence of UF in women of African ancestry is higher than that in other races.[4-6] For example, a large longitudinal study (Nurses' Health Study II) in the USA showed that the incidence of UF confirmed by pelvic examination, ultrasound (USS) or hysterectomy per 1000 woman-years was 37.9 in African American, 14.5 in Hispanic, 12.5 in White and 10.4 in Asian women.[5] In another longitudinal study conducted in United Kingdom, the crude incidence of UF based on primary care physicians' diagnosis with USS, hysteroscopy, laparoscopy or pelvic examination was 5.8 per 1000 woman-years.[7]

There are several epidemiological risk factors for UF. These include advanced age, race, age at menarche, low or nulliparity, family history, obesity, diet, physical activity, smoking, oral contraceptives, hormone replacement therapy, environmental exposure to high levels of estrogen and progesterone, and vitamin D deficiency.[3,8-10] Age is consistently associated with the incidence and prevalence of UF irrespective of ethnicity, race and other risk factors. In general, the risk of UF is about 4-11 times higher in women aged 40-60 years compared to 20-30 years old women and women older than 60 years.[1,3] Several studies show that early age at menarche is associated with higher risk

UF.[3,11,12] Multiparity is linearly associated with reduced risk of UF.[3,13] The risk reduction among multiparous women ranges from 20 to 50% compared to nulliparous women.[1]

Overweight and obesity are independent risk factors for UF.[14] A meta-analysis of 325,899 women among whom 19,593 had UF showed association with obesity.[14] The association was present whether obesity was assessed using waist-to-hip ratio (WHR), waist circumference, weight change from age 18 years, or body mass index (BMI).[14] Some studies found a dose response relationship between obesity and UF while other studies did not find such relationship.[3,14-16]

While few studies reported no associations between dietary intakes and UF, other studies showed a reduced risk with consumption of vegetables and fruits, and increased risk with intakes of food additives, sweeteners, soya milk and dietary fats.[1,14,17-19] Most studies found low level of serum vitamin D to be associated with increased risk of UF while a few reported no effect.[20,21] The association between vitamin D and UF was stronger in black compared to White women. Exposure to sunlight for more than an hour a day was also associated with reduced risk of UF.[20] Smoking was associated with reduced risk of UF, especially in women with low BMI.[1] Most studies reported an inverse relationship between regular physical activities and risk of UF.[3,19] Oral and injectable contraceptives use were associated with reduced risk of UF, however a few studies found increased or no risk in women using oral contraceptives.[1,3] Hormone replacement therapy or exposure to exogenous hormones, particularly among postmenopausal women was associated with increased risk of UF in some studies.[3]

Genetic and epigenetic factors have been associated with risk of UF. Positive family history is associated with increased risk of UF and higher risk was reported among sisters.[1,22-26] The estimates of heritability for UF were 26 to 69% in twin studies while data from GWAS reported heritability risk of 13%.[27,28] The risk of UF is 2.5-fold among first degree relatives compared with the general population.[28] The concordance rate of UF among monozygotic twins is twice that of dizygotic twins of the same sex, and a lot higher than in first-degree relatives.[28,29] Recently, genome wide association studies (GWAS) identified several candidate loci for UF in chromosome regions among African

American - 22q13.1 (*CYTH4*), Caucasian - 11p15.5 (*BETIL*), 17q25.3 (*FASN, CCDC57, and SLC16A3*), 22q13.1 (*TNRC6B*), and Asian - 10q24.33 (*OBFC1*), 11p15.5(*BET1L*), and 22q13.1 (*TNRC6B*) – populations.[30-33]

UF is associated with significant morbidity and substantial socio-economic costs.[34-36] Data from a global systematic review of the cost of UF showed that the total direct and indirect cost after diagnosis or from surgical care ranged from US$11,717 to 25,023 per patient per year.[37] In United States, the annual cost of UF to the economy was estimated to be between US$5.9 to 34.4 billion with obstetric complications contributing the highest fraction of the economic burden.[38]

Consistent with the high incidence and prevalence of UF in African populations in developed countries, case reports and clinical evidence suggest high prevalence of UF in black women living in Africa. However, in contrast to developed countries, there have been very few, adequately powered, systematic epidemiological studies of UF in Africa. In this scoping review of current publications on the epidemiology of UF in Africa, we aim to establish the state of the evidence and their limitations, the burden of UF and priorities for research on UF in black women living in SSA.

Methods

In this review, we used the Joanna Briggs Institute (JBI) guidelines for the conduct of systematic scoping review which was earlier described by Arksey and O'Malley.[39,40] Briefly, we base this review on five frameworks: (a) identifying the research question, (b) identifying the relevant studies (search strategy), (c) selecting the eligible studies, (d) charting the data and (e) collating, summarising, and reporting the results with or without consultation with experts on the specific field. [40]

Research question

The research questions for this scoping review are: What are the prevalence and incidence of UF among black women in SSA? What are the risk factors for UF among SSA women?

Information sources and search strategy

We conducted a systematic search of three online databases for records in English: PubMed, African Wide Information (EBSCO) and African Journal Online (AJOL). We used the following keywords to search the databases to retrieve published articles on the incidence, prevalence, and risk factors of UF; uterine fibroids or fibroids or leiomyoma or myoma; prevalence, incidence, risk factors or causes and Sub-Saharan Africa (SSA) (using sub-regions within SSA (West Africa OR East Africa OR Central Africa OR Southern Africa), and by specific country names) (Supplementary Table 1 – Search Term Strategy). We used Boolean terms AND/OR to separate the keywords during the search. We included Medical Subject Headings (MeSH) terms in the search terms. We also manually searched references and bibliography of relevant articles on this subject. The search was conducted between December 2019 and 27th January 2021.

Eligibility criteria

We used the PICO format (population, intervention, comparator, and outcome) to design the eligibility criteria for the studies that were included in this review. These are (a) published peer reviewed article with observational or experimental design that reported on the aetiology or risk factors or incidence or prevalence or proportion of women with UFs and (b) data must have been collected in SSA among

indigenous black women population. We excluded case reports, letter to editors or expert opinion without primary data on UFs in SSA as well as studies that only reported the outcome of treatment.

Study Selection process

All titles retrieved from searches were compiled and reviewed with Endnote X 8.0 (Thompson Reuters). We removed all duplicates using the Endnote automated system and manually. We screened abstracts in accordance with our inclusion and exclusion criteria. Next, we screened the full texts of abstracts that were eligible for further consideration. Only articles that met the inclusion criteria during full text screening were finally selected for data charting in this review.

Charting data

We entered our data into a prepared Microsoft Excel sheet using the following data charting fields: authors, date, country, study design, aim/objectives, sample size, recruitment strategy (probability or non-probability sampling), study settings (health facility/community/online), outcome measured (prevalence/incidence/proportion), analysis (descriptive/test of association/multivariable analysis) and summary of key findings (Table 1).

Collating, summarising, and reporting the results

We present a descriptive summary of eligible studies and we created a Prisma-ScR flow chart to summarise the process and number of articles that were finally selected for data charting (Supplementary Table 2).[41] The chart shows the overall number of studies included, study designs and settings, publication years, the characteristics of the study populations, the outcomes reported, and the countries where the studies were conducted. In line with scoping reviews' methodology, we did not perform an assessment of the quality of the included studies.

Patient and Public Involvement

It was not possible to describe patient and public involvement in this research.

Results

We retrieved 1,052 studies from the three databases (Figure 1). After removal of duplicate publications, we screened 484 titles and abstracts and found only 48 articles were eligible for full-text screening. We excluded 39 of the 48 full text articles because 17 of them were on symptoms/management of UF, 7 were animal studies, 5 each were case reports and reviews, 2 were from outside SSA, 1 each were on recurrent UF after treatment, full texts not available and on somatic genetic mutation in UF. Of the 9 studies that met the inclusion criteria, 4 were from Nigeria,[42-45] 2 from Ghana,[46,47] and 1 study each from Cameroon,[48] Kenya[49] and South Africa.[50]

Incidence or prevalence of UF

Five of the 9 studies screened described the prevalence of UF (Table 1).[42,44,46,48,50] Two of these studies, one each from pathology departments in single institutions in South Africa and Nigeria, examined the proportion of UF in surgical specimens.[42,50] In Northern Nigeria, UF accounted for 2.2% of all surgical specimen at a single facility over a five-year period.[42] The South African study reported that the proportion of UF among all hysterectomy specimens in a single institution over a six-month period was 64.6%.[50]

A cross-sectional study of pregnant women undergoing abdominal USS examination in two regional hospitals in Cameroun reported that 16.8% (38/226) had UF.[48] Another cross-sectional study in Ghana among 244 non-pregnant women referred for abdominal USS showed that 36.9% had UF and the proportion of women with UF increased with age.[46] A 2-year retrospective review of attendees at the gynaecology clinic of a public tertiary health institution in Nigeria showed that 30.7% (178/580) of all patients had a diagnosis of UF.[44] Another study of pregnant women referred for prenatal abdominal USS at a tertiary hospital in eastern Nigeria showed that the prevalence of UF was 12.3% during pregnancy.[43]

Role of Oestrogen, Progesterone, and their receptors

A study in Kenya reported on cytosolic quantification of oestrogen and progesterone and their receptors in UF tissue measured using radioimmunoassay.[49] The study showed that UF contained lower levels of oestrogen and progesterone but higher levels of receptors for these hormones compared to normal uterine tissue.[49] In a more recent Nigerian study using immunohistochemistry, the level of oestrogen and progesterone receptors in UF was higher than in uterine tissue.[45] The Nigerian study further showed a significant negative correlation between UF size and the progesterone receptors levels only (Table 1).[45]

Risk factors for UF

Three studies presented data on risk factors of UF (Tables 1 and 2).[44,46,48] In a Nigerian case-control study of gynaecology clinic attendees, advanced age (OR=4.90; 95%CI 1.80-31.1) and positive family history (OR=3.0; 95%CI 1.90-4.80) were associated with higher risk while obesity (OR=0.4; 95%CI 0.10-0.90) and primiparity (OR=0.60; 95%CI 0.20-0.90) were associated with lower risk of UF.[44] A cross-sectional study of 244 women referred for abdominal USS at three centres in Ghana found that women with UF tended to be older (p=0.001), obese (0.001), older at last pregnancy and delivery (p=0.001) and have lower parity (p=0.001). [46] In another cross-sectional study of factors associated with UF in pregnancy in Cameroun, women with UF were older (p<0.001) and had higher gravidity (p=0.02). [48]

Discussion

In this review, we mapped published epidemiological studies on incidence, prevalence, and risk factors for UF in indigenous African women. Our results confirmed the paucity of systematic epidemiological study of UF among black women in Africa. Only few studies have some information on prevalence/proportion of, and risk factors for UF.[42,44,46,48,50] The five studies that reported the prevalence of UF used different populations, denominators, and study designs.[42,44,46,48,50] Two studies from pathology departments in Nigeria and South Africa used different reporting periods and denominators to calculate the proportions of UF.[42,50] We also observed variations in the reporting of the prevalence of UF in pregnancy in the two studies from radiology departments in Nigeria and Cameroon.[43,48] They both used convenience sampling technique and were silent on the gestational ages of participants. The only Nigerian study that presented data on the prevalence of UF among non-pregnant women was a retrospective review of case records that used all other attendees at a gynaecological clinic as controls.[44] There was no study in this review that has information on the incidence of UF in pregnant or non-pregnant women.

Two studies were on the role of oestrogen and progesterone and their receptors. The two hormonal studies used different diagnostic techniques (radioimmunoassay versus immunochemistry), laboratory estimation of cut-off levels for oestrogen and progesterone and comparator groups (UF and normal myometrial tissue from same patient versus UF and normal myometrial tissue from different patients as cases and control).[45,49] The observed differences in the methodology of the two studies make it difficult to compare and interpret their findings. We observed that the sample sizes of these three studies were too small to allow for rigorous multivariable analysis for confounders. In addition, the three studies were conducted with specimen from women who had treatment in specific health facilities.

Three studies described risk factors for UF among black African women, but they all used different research designs and data analysis techniques.[44,46,48] All the studies were conducted within single

facilities, two were cross-sectional and one was a retrospective case control study. The risk factors identified in the three studies were similar to those reported in studies conducted in USA, Europe and Asia. [5,12,51] Briefly, advancing age was the only risk factors that was common to all three studies and low parity was reported in two studies.[44,46,48] The only other risk factor reported among non-pregnant women was self-report of family history of UF.[44] Obesity was reported as a protective factor in non-pregnant Nigerian women and as a risk factor in pregnant women in Ghana.[44,48] The tests for association in these studies were not well described in the methods sections of their manuscripts.[44,46,48] The studies from Cameroon and Ghana used bivariate tests and did not adjust for age in their analyses.[46,48] The only Nigerian study that used multivariable analysis to adjust for confounders, used data collected from a retrospective review of cases managed in a tertiary public health facility and assigned other attendees as controls.[44]

Although, we did not assess the risk of bias in studies that we reviewed because that is outside the objective of scoping review generally, we observed that the majority of the studies used data collected from case series or cross-sectional studies (6/9) while two (3/9) were case control studies.[42-50] None of the 9 studies we reviewed used probability sampling technique to select their subjects and only one study reported on sample size and power calculation.

We found several gaps in the epidemiology of UF in SSA. There was no genomic epidemiology study of uterine fibroid in SSA. Studies from high income countries have shown that only 20.0-40.0% of women with symptomatic UF seek medical treatment, suggesting that a significant number of women with UF are not captured by facilities based studies.[52] We did not find any published population based study with adequate statistical power and sampling strategy which can generate generalizable information on incidence, prevalence and risk factors of UF among indigenous black African women. There are many epidemiological risk factors of UF that are yet to be investigated in SSA. These factors include reproductive factors (age at menarche and menopause, birth interval or inter pregnancy interval, contraceptives, and hormone replacement therapy), diets including vitamin D, trace elements

and heavy metals, lifestyle and physical activity, reproductive tract infections, microbiome, and pollution. [3,8,12,53,54] Lack of information on these risk factors prevent development of preventive and therapeutic interventions. This is a serious gap in knowledge considering the morbidity, mortality, and economic costs of UF in SSA.

The interpretation of findings from this scoping review may be limited for the following reasons. We searched published articles from online databases only. We may have missed papers published in journals that are not indexed in these online databases. We excluded one article that we could not retrieve the full texts, but the abstract shows that this was on the association between UF and BMI. Despite these limitations, this scoping review confirmed the dearth of studies on the epidemiology of UF among SSA women and argues for urgent remediation of this situation.

Conclusions

Our results show that there is limited information on the epidemiology of UF and identified gaps in knowledge of UF among women in SSA despite its high prevalence, morbidity, and economic costs. We recommend urgent implementation of well-designed and adequately powered studies to address this gap.

Authors' contribution: CAA conceived and designed the study. He conducted literature review, reviewed, revised, and approved the manuscript. IMB participated in the design, conducted literature search, screening of articles and data charting. He wrote the first draft, revised, and approved the manuscript.

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References:

1. Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. *BJOG* 2017; **124**(10): 1501-12.

2. Holdsworth-Carson SJ, Zaitseva M, Vollenhoven BJ, Rogers PA. Clonality of smooth muscle and fibroblast cell populations isolated from human fibroid and myometrial tissues. *Molecular human reproduction* 2014; **20**(3): 250-9.

3. Wise LA, Laughlin-Tommaso SK. Epidemiology of Uterine Fibroids: From Menarche to Menopause. *Clin Obstet Gynecol* 2016; **59**(1): 2-24.

4. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol* 2003; **188**(1): 100-7.

5. Marshall LM, Spiegelman D, Barbieri RL, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstet Gynecol* 1997; **90**(6): 967-73.

6. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Age-specific incidence rates for self-reported uterine leiomyomata in the Black Women's Health Study. *Obstet Gynecol* 2005; **105**(3): 563-8.

7. Martin-Merino E, Wallander MA, Andersson S, Soriano-Gabarro M, Rodriguez LA. The reporting and diagnosis of uterine fibroids in the UK: an observational study. *BMC Womens Health* 2016; **16**: 45.

8. Brakta S, Diamond JS, Al-Hendy A, Diamond MP, Halder SK. Role of vitamin D in uterine fibroid biology. *Fertil Steril* 2015; **104**(3): 698-706.

9. Baird DD, Harmon QE, Upson K, et al. A Prospective, Ultrasound-Based Study to Evaluate Risk Factors for Uterine Fibroid Incidence and Growth: Methods and Results of Recruitment. *Journal of women's health* 2015; **24**(11): 907-15.

10. Wise LA, Palmer JR, Rosenberg L, Haddad SA, Ruiz-Narvaez EA. FASN, dietary fat intake, and risk of uterine leiomyomata in the Black Women's Health Study. *Fertil Steril* 2016; **106**(5): 1136-41.

11. Styer AK, Rueda BR. The Epidemiology and Genetics of Uterine Leiomyoma. *Best practice & research Clinical obstetrics & gynaecology* 2016; **34**: 3-12.

12. Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. *Int J Fertil Steril* 2016; **9**(4): 424-35.

13. Baird DD, Dunson DB. Why is parity protective for uterine fibroids? *Epidemiology* 2003; **14**(2): 247-50.

14. Qin H, Lin Z, Vásquez E, Luan X, Guo F, Xu L. Association between obesity and the risk of uterine fibroids: a systematic review and meta-analysis. *J Epidemiol Community Health* 2021; **75**(2): 197-204.

15. Lee JE, Song S, Cho E, et al. Weight change and risk of uterine leiomyomas: Korea Nurses' Health Study. *Curr Med Res Opin* 2018; **34**(11): 1913-9.

16. Sato F, Nishi M, Kudo R, Miyake H. Body fat distribution and uterine leiomyomas. *J Epidemiol* 1998; **8**(3): 176-80.

17. Shen Y, Xu Q, Xu J, Ren ML, Cai YL. Environmental exposure and risk of uterine leiomyoma: an epidemiologic survey. *Eur Rev Med Pharmacol Sci* 2013; **17**(23): 3249-56.

18. Wise LA, Radin RG, Kumanyika SK, Ruiz-Narvaez EA, Palmer JR, Rosenberg L. Prospective study of dietary fat and risk of uterine leiomyomata. *Am J Clin Nutr* 2014; **99**(5): 1105-16.

19. He Y, Zeng Q, Dong S, Qin L, Li G, Wang P. Associations between uterine fibroids and lifestyles including diet, physical activity and stress: a case-control study in China. *Asia Pac J Clin Nutr* 2013; **22**(1): 109-17.

20. Baird DD, Hill MC, Schectman JM, Hollis BW. Vitamin d and the risk of uterine fibroids. *Epidemiology* 2013; **24**(3): 447-53.

21. Ciebiera M, Włodarczyk M, Ciebiera M, Zaręba K, Łukaszuk K, Jakiel G. Vitamin D and uterine fibroids—review of the literature and novel concepts. *International journal of molecular sciences* 2018; **19**(7): 2051.

22. D'Aloisio AA, Baird DD, DeRoo LA, Sandler DP. Early-life exposures and early-onset uterine leiomyomata in black women in the Sister Study. *Environ Health Perspect* 2012; **120**(3): 406-12.

23. Mu X, Du X, Yao K, et al. Association between HSD17B1 rs605059 polymorphisms and the risk of uterine diseases: a systemic review and meta-analysis. *International journal of clinical and experimental pathology* 2015; **8**(6): 6012-8.

24. Bideau VS, Alleyne AT. Leu/Val SNP polymorphism of CYP1B1 and risk of uterine leiomyoma in a Black population. *Tumour Biol* 2016; **37**(3): 4035-40.

25. Gallagher CS, Morton CC. Genetic Association Studies in Uterine Fibroids: Risk Alleles Presage the Path to Personalized Therapies. *Seminars in reproductive medicine* 2016; **34**(4): 235-41.

26. Aissani B, Zhang K, Wiener H. Genetic determinants of uterine fibroid size in the multiethnic NIEHS uterine fibroid study. *Int J Mol Epidemiol Genet* 2015; **6**(1): 9-19.

27. Ponomarenko I, Reshetnikov E, Polonikov A, et al. Candidate Genes for Age at Menarche Are Associated With Uterine Leiomyoma. *Front Genet* 2020; **11**: 512940.

28. Luoto R, Kaprio J, Rutanen EM, Taipale P, Perola M, Koskenvuo M. Heritability and risk factors of uterine fibroids--the Finnish Twin Cohort study. *Maturitas* 2000; **37**(1): 15-26.

29. Vikhlyaeva EM, Khodzhaeva ZS, Fantschenko ND. Familial predisposition to uterine leiomyomas. *Int J Gynaecol Obstet* 1995; **51**(2): 127-31.

30. Hellwege JN, Jeff JM, Wise LA, et al. A multi-stage genome-wide association study of uterine fibroids in African Americans. *Hum Genet* 2017; **136**(10): 1363-73.

31. Edwards TL, Michels KA, Hartmann KE, Velez Edwards DR. BET1L and TNRC6B associate with uterine fibroid risk among European Americans. *Hum Genet* 2013; **132**(8): 943-53.

32. Cha P-C, Takahashi A, Hosono N, et al. A genome-wide association study identifies three loci associated with susceptibility to uterine fibroids. *Nature genetics* 2011; **43**(5): 447-50.

33. Eggert SL, Huyck KL, Somasundaram P, et al. Genome-wide linkage and association analyses implicate FASN in predisposition to uterine leiomyomata. *The American Journal of Human Genetics* 2012; **91**(4): 621-8.

34. Agboola AD, Bello OO, Olayemi OO. A clinical audit of the patterns of presentations and complications of abdominal myomectomy at the University College Hospital, Ibadan, Nigeria. *J Obstet Gynaecol* 2021: 1-6.

35. Yorgancı A, Meydanlı MM, Kadıoğlu N, et al. Incidence and outcome of occult uterine sarcoma: A multi-centre study of 18604 operations performed for presumed uterine leiomyoma. *J Gynecol Obstet Hum Reprod* 2020; **49**(1): 101631.

36. Foth D, Rohl FW, Friedrich C, et al. Symptoms of uterine myomas: data of an epidemiological study in Germany. *Arch Gynecol Obstet* 2017; **295**(2): 415-26.

37. Soliman AM, Yang H, Du EX, Kelkar SS, Winkel C. The direct and indirect costs of uterine fibroid tumors: a systematic review of the literature between 2000 and 2013. *American journal of obstetrics and gynecology* 2015; **213**(2): 141-60.

38. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol* 2012; **206**(3): 211 e1-9.

39. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis, JBI, 2020. Available from https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-20-12. 2020.

40. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International journal of social research methodology* 2005; **8**(1): 19-32.

41. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of Internal Medicine* 2018; **169**(7): 467-73.

42. Mohammed A, Shehu S, Ahmed S, et al. Uterine leiomyomata: a five year clinicopathological review in Zaria, Nigeria. *Nigerian Journal of surgical research* 2005; **7**(1): 206-8.

43. Eze CU, Odumeru E, Ochie K, Nwadike U, Agwuna K. Sonographic assessment of pregnancy co-existing with uterine leiomyoma in Owerri, Nigeria. *African Health Sciences* 2013; **13**(2): 453-60.

44. Oluwole A, Owie E, Babah O, Afolabi B, Oye-Adeniran B. Epidemiology of Uterine Leiomyomata at the Lagos University Teaching Hospital, Idi-Araba, Lagos. *Nigerian Hospital Practice* 2015; **15**(1-3): 14-20.

45. Awowole IO, Makinde ON, Badejoko OO, et al. Clinical correlates of leiomyoma estrogen and progesterone receptors among Nigerian women. *International Journal of Gynecology & Obstetrics* 2016; **135**(3): 314-8.

46. Sarkodie BD, Botwe BO, Adjei DN, Ofori E. Factors associated with uterine fibroid in Ghanaian women undergoing pelvic scans with suspected uterine fibroid. *Fertility research and practice* 2016a; **2**(1): 1-7.

47. Sarkodie BD, Botwe BO, Ofori EK. Uterine fibroid characteristics and sonographic pattern among Ghanaian females undergoing pelvic ultrasound scan: a study at 3-major centres. *BMC women's health* 2016b; **16**(1): 1-6.

48. Egbe TO, Badjang TG, Tchounzou R, Egbe E-N, Ngowe MN. Uterine fibroids in pregnancy: prevalence, clinical presentation, associated factors and outcomes at the Limbe and Buea Regional Hospitals, Cameroon: a cross-sectional study. *BMC research notes* 2018; **11**(1): 1-6.

49. Wango EO, Tabifor HN, Muchiri LW, Sekadde-Kigondu C, Makawiti DW. Progesterone, estradiol and their receptors in leiomyomata and the adjacent normal myometria of black Kenyan women. *African journal of health sciences* 2002; **9**(2): 123-8.

50. Tiltman AJ. Leiomyomas of the uterine cervix: a study of frequency. *International journal of gynecological pathology: official journal of the International Society of Gynecological Pathologists* 1998; **17**(3): 231-4.

51. Wise LA, Palmer JR, Harlow BL, et al. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African-American women: a prospective study. *Am J Epidemiol* 2004; **159**(2): 113-23.

52. Marsh EE, Ekpo GE, Cardozo ER, Brocks M, Dune T, Cohen LS. Racial differences in fibroid prevalence and ultrasound findings in asymptomatic young women (18-30 years old): a pilot study. *Fertil Steril* 2013; **99**(7): 1951-7.

53. Hansen JG, Tang W, Hootman KC, et al. Genetic and environmental factors are associated with serum 25-hydroxyvitamin D concentrations in older African Americans. *J Nutr* 2015; **145**(4): 799-805.

54. Moore KR, Cole SR, Dittmer DP, Schoenbach VJ, Smith JS, Baird DD. Self-Reported Reproductive Tract Infections and Ultrasound Diagnosed Uterine Fibroids in African-American Women. *Journal of women's health* 2015; **24**(6): 489-95.

Table 1: Descriptive analysis of studies included in the scoping review

Author; Year	Reference	Research focus	Study design	Sampling methods	Sample size	Outcome measured	Age of study participants	Summary of key findings
Tiltman et. al. 1998 [South Africa]	50	Pathology	Case series	Non-probability	661	Proportion of UF within hysterectomy specimen	12.0-84.0	The proportion of UF was 427/661 (64.6%)
Wango et. al. 2002 [Kenya]	49	Pathology	Case series	Not clearly described	20	Evaluation of estradiol, progesterone, and their receptors	Range 31.0-42.0	The UF tissue contained significantly higher levels of estrogen receptor (28.2±1.6 vs 19.1±0.4 fm/mg protein) and progesterone receptor (16.8±0.7 vs 9.4±0.2 fm/mg protein) compared to normal myometrial tissue, a relatively significant higher levels of estrogen (1117.6±20.9 vs 616.9±19.8 pm/mg protein) and progesterone (7.7±0.25 vs 3.2±0.34 nm/mg protein) in the myometrium than in the leiomyomata.
Mohammed et. al. 2005 [Nigeria]	42	Pathology	Case series	Non-probability	209	Proportion of UF pathological specimen & degenerative changes	Range 25.0-50.0	The proportion of myometrial UF was 2.2% of all surgical specimen over five years.
Eze et. al. 2013 [Nigeria]	43	Radiology	Case control	Non-probability	200 (100 cases vs 100 controls)	Frequency and growth rate of uterine fibroids in pregnancy	Cases (31.6 ± 4.5yr); Controls (29.1 ± 5.5yr)	The frequency of UFs in pregnancy was 12.3%; the commonest type was subserous fibroids (27.5%). The mean size of UFs measured on ultrasound was lowest during third scan.
Oluwole et. al. 2015 [Nigeria]	44	Clinical	Case control	Non-probability	580	Proportion of UF & risk factor analysis	35.5±5.8	The proportion of women with UFs was 31% (178/580). Presence of UFs was associated with 40-49years (OR=4.9%; 95%CI 1.8-31.1); lower parity (OR=0.6; 95%CI 0.2-0.9); family history of UFs (OR=1.9; 95%CI 1.9-4.8); and history of infertility (OR=5.0; 95%CI 0.9-25.9)
Awowole et. al. 2016 [Nigeria]	45	Pathology	Cross-sectional	Non-probability	60	To measure expression of estrogen receptor α (ERα) and progesterone receptor (PR) in myometrium and UF	26.0-53.0	UF had a higher mean expression of estrogen receptor (Erα) (H-score 193.4 ± 64.6 vs 153.3 ± 69.1; p = 0.01) and progesterone receptor (PR) (214.9 ± 66.6 vs 171.5 ± 63.5; p < 0.001) than in myometrial tissues. The tumor diameter correlated negatively with the immunoscores of both receptors irrespective of age, parity, and body mass index, but this was only significant for PR (p = –0.44; p<0.001).
Sarkodie et. al. 2016a [Ghana]	46	Radiology	Cross-sectional	Non-probability	244	Prevalence of UF & risk factors analysis	14.0-54.0	In this study, 23 % (38/168) of women <35 had prevalent fibroids, compared to 67 % (36/54) of

								women 35–44, and 73 % (16/22) of women at 45 or above years. Factors that associated significantly with UF in Ghanaian women included obesity (X2 = 17.3, p-value = 0.001), participant's age range (X2 = 47.4, p = 0.001), parity (X2 = −10.2, p = 0.001), and age at last delivery (X2 = 34.6, p = 0.001).
Sarkodie et. al. 2016b [Ghana]	47	Radiology	Cross-sectional	Non-probability	244	Assessment of sonographic characteristics of UF	14.0-54.0	The prevalence of UF was 36.9 % (90/244). The majority of the UFs were intramural (57.8 %) with only 4.4 % noted as sub-mucosal. Most (55.6 %) of the UFs were located in more than one part of the uterus.
Egbe et. al. 2018 [Cameroon]	48	Radiology & Clinical	Cross-sectional	Non-probability	226	Proportion of UF & risk factors analysis	≥21.0	The prevalence of UF in pregnancy was 16.7% (38/226). Respondents with UF were older than those without (p < 0.001) and of low parity (p = 0.02).

UF – Uterine Fibroids; CI – Confidence interval; OR – Odds ratio

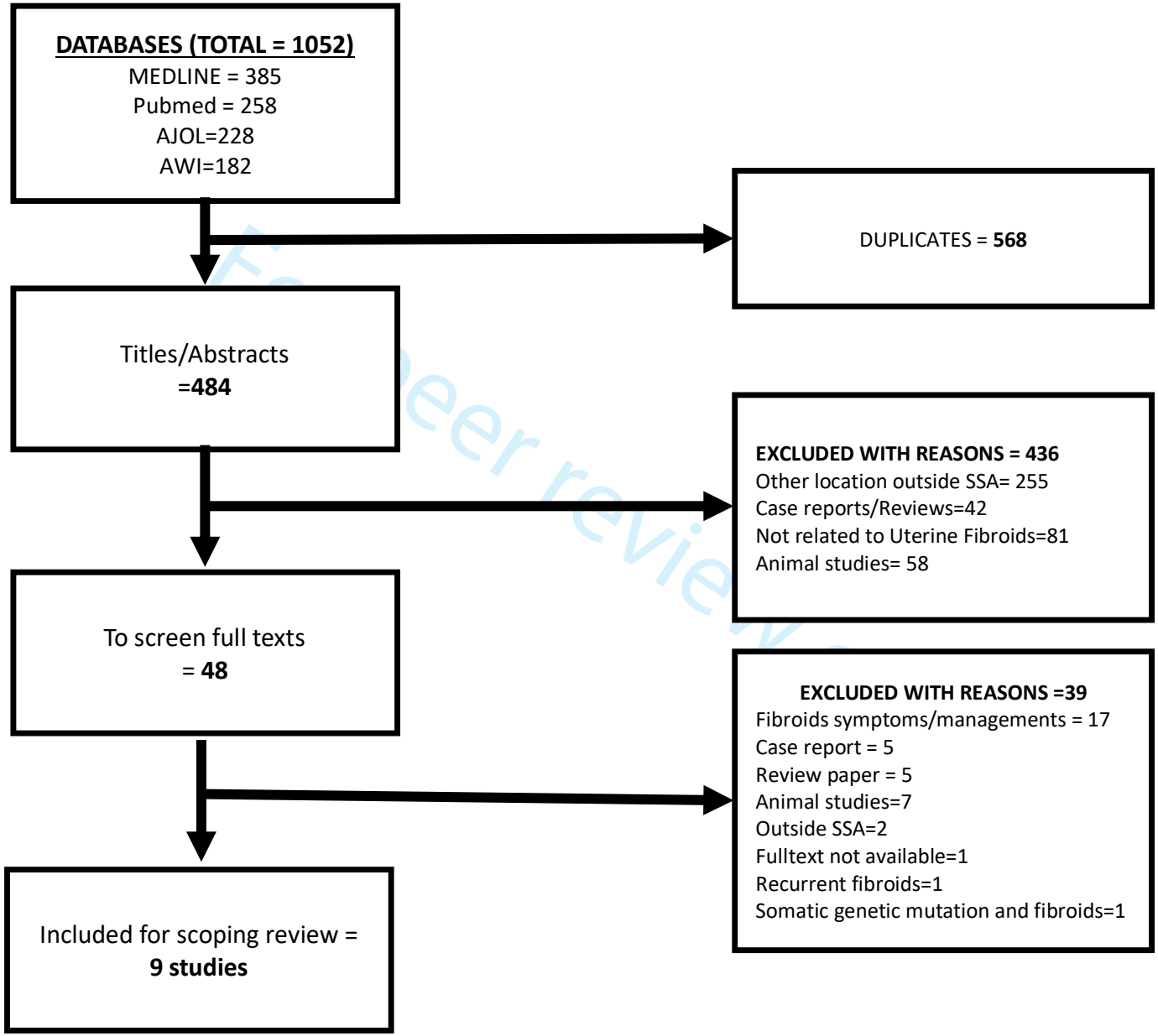
Table 2: Summary of reported risk factors associated with UF in SSA

Risk factors	Pregnant women		Non-Pregnant women
	Egbe et. al. 2018 [Cross-sectional study from Cameroon]	**Sarkodie et. al. 2016a [Cross-sectional study from Ghana]**	**Oluwole et. al. 2015 [Case control study from Nigeria]**
Advanced age	↑	↑	↑
Family history	Not considered	Not considered	↑
Obesity	Not considered	↑	↓
Nulliparity	Not considered	↑	Not considered
Gravidity	↑	Not considered	Not considered
Advanced age at delivery	Not considered	↑	Not considered
At least primiparity	Not considered	Not considered	↓

↑ - Increased risk, ↓ - Decreased risk, Not considered as a risk factor in the study

Figure 1: The Prisma Flow Chart for the scoping review

Figure 1: The Prisma Flow Chart



Supplementary Table 1: Search Strategy used for PubMED

CONCEPTS	SN	TERMS	SEARCH DETAILS
Concept 1: Uterine fibroids	#1	uterine fibroids	"leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR ("uterine"[All Fields] AND "fibroids"[All Fields]) OR "uterine fibroids"[All Fields] OR ("fibroid s"[All Fields] OR "leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "fibroid"[All Fields] OR "fibroids"[All Fields])
	#2	fibroids	fibroids"[All Fields] OR "leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "fibroid"[All Fields] OR "fibroids"[All Fields]
	#3	leiomyoma	leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "leiomyomas"[All Fields] OR "myoma"[MeSH Terms] OR "myoma"[All Fields] OR "myomas"[All Fields] OR "myoma s"[All Fields]
	#4	myoma	"leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "leiomyomas"[All Fields] OR "myoma"[MeSH Terms] OR "myoma"[All Fields] OR "myomas"[All Fields] OR "myoma s"[All Fields]
	#5	**#1 OR #2 OR #3 OR #4**	
Concept 2: Epidemiological indicators/measure used	#6	Cause OR causes	"causative"[All Fields] OR "causatively"[All Fields] OR "causatives"[All Fields] OR "cause"[All Fields] OR "caused"[All Fields] OR "causing"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causes"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields] OR "causative"[All Fields] OR "causatively"[All Fields] OR "causatives"[All Fields] OR "cause"[All Fields] OR "caused"[All Fields] OR "causing"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causes"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields]
	#7	aetiology OR etiology	"aetiologie"[All Fields] OR "aetiologies"[All Fields] OR "aetiology"[All Fields] OR "etiologies"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields] OR "aetiologie"[All Fields] OR "aetiologies"[All Fields] OR "aetiology"[All Fields] OR "etiologies"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields]
	#8	Risk factor	"risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk factors"[All Fields] OR ("risk"[All Fields] AND "factor"[All Fields]) OR "risk factor"[All Fields]
	#9	Prevalence OR prevalen*	"epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields]
	#10	Incidence OR inciden*	"epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "incidence"[All Fields] OR "incidence"[MeSH Terms] OR "incidences"[All Fields] OR "incident"[All Fields] OR "incidents"[All Fields]
	#11	epidemiology	"epidemiologies"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "epidemiology"[MeSH Terms] OR "epidemiology s"[All Fields]
	#12	**#6 OR #7 OR #8 OR #9 OR #10 OR #11**	
Concept 3: Women	#13	Women OR Woman	"womans"[All Fields] OR "women"[MeSH Terms] OR "women"[All Fields] OR "woman"[All Fields] OR "women s"[All Fields] OR "womens"[All Fields]
	#14	**#13**	
Concept 4: Sub-Saharan Africa	#15	Africa	"africa"[MeSH Terms] OR "africa"[All Fields] OR "africa s"[All Fields] OR "africas"[All Fields]
	#16	West Africa	"africa, western"[MeSH Terms] OR ("africa"[All Fields] AND "western"[All Fields]) OR "western africa"[All Fields] OR ("west"[All Fields] AND "africa"[All Fields]) OR "west africa"[All Fields]
	#17	East Africa	"africa, eastern"[MeSH Terms] OR ("africa"[All Fields] AND "eastern"[All Fields]) OR "eastern africa"[All Fields] OR ("east"[All Fields] AND "africa"[All Fields]) OR "east africa"[All Fields]
	#18	Central Africa	"africa, central"[MeSH Terms] OR ("africa"[All Fields] AND "central"[All Fields]) OR "central africa"[All Fields] OR ("central"[All Fields] AND "africa"[All Fields])
	#19	Southern Africa	"africa, southern"[MeSH Terms] OR ("africa"[All Fields] AND "southern"[All Fields]) OR "southern africa"[All Fields] OR ("southern"[All Fields] AND "africa"[All Fields])
	#20	Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cameroon OR Cape Verde OR Central	"angola"[MeSH Terms] OR "angola"[All Fields] OR "angola s"[All Fields] OR ("benin"[MeSH Terms] OR "benin"[All Fields] OR "benin s"[All Fields]) OR ("botswana"[MeSH Terms] OR "botswana"[All Fields] OR "botswana s"[All Fields]) OR ("burkina faso"[MeSH Terms] OR ("burkina"[All Fields] AND

		African Republic OR Chad OR Comoros OR Côte d'Ivoire OR Democratic Republic of the Congo OR Djibouti OR Equatorial Guinea Eritrea OR Ethiopia OR Gabon OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Republic of the Congo OR Rwanda OR São Tomé and Príncipe OR Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR South Sudan OR Swaziland OR Tanzania OR The Gambia OR Togo OR Uganda OR Zambia OR Zimbabwe	"faso"[All Fields]) OR "burkina faso"[All Fields]) OR ("burundi"[MeSH Terms] OR "burundi"[All Fields]) OR ("cameroon"[MeSH Terms] OR "cameroon"[All Fields] OR "cameroons"[All Fields] OR "cameroon s"[All Fields]) OR ("cabo verde"[MeSH Terms] OR ("cabo"[All Fields] AND "verde"[All Fields]) OR "cabo verde"[All Fields] OR ("cape"[All Fields] AND "verde"[All Fields]) OR "cape verde"[All Fields]) OR ("central african republic"[MeSH Terms] OR ("central"[All Fields] AND "african"[All Fields] AND "republic"[All Fields]) OR "central african republic"[All Fields]) OR ("chad"[MeSH Terms] OR "chad"[All Fields]) OR ("comoros"[MeSH Terms] OR "comoros"[All Fields] OR "comoro"[All Fields]) OR ("cote d ivoire"[MeSH Terms] OR ("cote"[All Fields] AND "d ivoire"[All Fields]) OR "cote d ivoire"[All Fields]) OR ("democratic republic of the congo"[MeSH Terms] OR ("democratic"[All Fields] AND "republic"[All Fields] AND "congo"[All Fields]) OR "democratic republic of the congo"[All Fields]) OR ("djibouti"[MeSH Terms] OR "djibouti"[All Fields]) OR (("equatorial guinea"[MeSH Terms] OR ("equatorial"[All Fields] AND "guinea"[All Fields]) OR "equatorial guinea"[All Fields]) AND ("eritrea"[MeSH Terms] OR "eritrea"[All Fields])) OR ("ethiopia"[MeSH Terms] OR "ethiopia"[All Fields] OR "ethiopia s"[All Fields]) OR ("gabon"[MeSH Terms] OR "gabon"[All Fields]) OR ("ghana"[MeSH Terms] OR "ghana"[All Fields] OR "ghana s"[All Fields]) OR ("guinea"[MeSH Terms] OR "guinea"[All Fields] OR "guinea s"[All Fields] OR "guineas"[All Fields]) OR ("guinea bissau"[MeSH Terms] OR "guinea bissau"[All Fields] OR ("guinea"[All Fields] AND "bissau"[All Fields]) OR "guinea bissau"[All Fields]) OR ("kenya"[MeSH Terms] OR "kenya"[All Fields] OR "kenya s"[All Fields]) OR ("lesotho"[MeSH Terms] OR "lesotho"[All Fields]) OR ("liberia"[MeSH Terms] OR "liberia"[All Fields] OR "liberia s"[All Fields]) OR ("madagascar"[MeSH Terms] OR "madagascar"[All Fields] OR "madagascar s"[All Fields]) OR ("malawi"[MeSH Terms] OR "malawi"[All Fields] OR "malawi s"[All Fields]) OR ("mali"[MeSH Terms] OR "mali"[All Fields]) OR ("mauritania"[MeSH Terms] OR "mauritania"[All Fields]) OR ("mauritius"[MeSH Terms] OR "mauritius"[All Fields]) OR ("mozambique"[MeSH Terms] OR "mozambique"[All Fields] OR "mozambique s"[All Fields]) OR ("namibia"[MeSH Terms] OR "namibia"[All Fields]) OR ("niger"[MeSH Terms] OR "niger"[All Fields]) OR ("nigeria"[MeSH Terms] OR "nigeria"[All Fields] OR "nigeria s"[All Fields]) OR ("congo"[MeSH Terms] OR "congo"[All Fields] OR ("republic"[All Fields] AND "congo"[All Fields]) OR "republic of the congo"[All Fields]) OR ("rwanda"[MeSH Terms] OR "rwanda"[All Fields] OR "rwanda s"[All Fields]) OR ("sao tome and principe"[MeSH Terms] OR ("sao"[All Fields] AND "tome"[All Fields] AND "principe"[All Fields]) OR "sao tome and principe"[All Fields]) OR ("senegal"[MeSH Terms] OR "senegal"[All Fields] OR "senegal s"[All Fields]) OR ("seychelles"[MeSH Terms] OR "seychelles"[All Fields]) OR ("sierra leone"[MeSH Terms] OR ("sierra"[All Fields] AND "leone"[All Fields]) OR "sierra leone"[All Fields]) OR ("somalia"[MeSH Terms] OR "somalia"[All Fields]) OR ("south africa"[MeSH Terms] OR ("south"[All Fields] AND "africa"[All Fields]) OR "south africa"[All Fields]) OR ("south sudan"[MeSH Terms] OR ("south"[All Fields] AND "sudan"[All Fields]) OR "south sudan"[All Fields]) OR ("eswatini"[MeSH Terms] OR "eswatini"[All Fields] OR "swaziland"[All Fields]) OR ("tanzania"[MeSH Terms] OR "tanzania"[All Fields] OR "tanzania s"[All Fields]) OR ("gambia"[MeSH Terms] OR "gambia"[All Fields] OR "the gambia"[All Fields]) OR ("togo"[MeSH Terms] OR "togo"[All Fields]) OR ("uganda"[MeSH Terms] OR "uganda"[All Fields] OR "uganda s"[All Fields]) OR ("zambia"[MeSH Terms] OR "zambia"[All Fields] OR "zambia s"[All Fields]) OR ("zimbabwe"[MeSH Terms] OR "zimbabwe"[All Fields] OR "zimbabwe s"[All Fields])
	#21	**#15 OR #16 OR #17 OR #18 OR #19 OR #20**	
Final Combined Terms	**#23**	**#5 AND #12 AND #14 AND #21**	

These search terms were used in the 3 databases (MEDLINE/PubMed, AJOL &AWI)

Supplementary Table 2: Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	#1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	#2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	#3, 4, & 5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	#6 & 7
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	Not done
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	#7 & 8
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	#7
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	# 7 [Supplement Table 2]
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	#8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	#8
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	#8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	#8
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	#8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	#9
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	#9 & 10
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	#9 & 10
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	#9 & 10
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	#9 & 10
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	#11, 12 & 13

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Limitations	20	Discuss the limitations of the scoping review process.	#13
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	#13
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	#14

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.
* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.
† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).
‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

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Systematic scoping review of the epidemiology of Uterine Fibroid in Black African women

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Systematic scoping review of the epidemiology of Uterine Fibroid in Black African women

Imran O. Morhason-Bello[1,2] Clement A. Adebamowo[3-4]

[1]Department of Obstetrics and Gynaecology, Faculty of Clinical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria
[2]Institute of Advanced Medical Research and Training, College of Medicine, University of Ibadan, Nigeria
[3]Center for Bioethics and Research, Ibadan, Nigeria
[4]Department of Epidemiology and Public Health; and Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Baltimore, MD

Corresponding author:
Clement Adebamowo MD, ScD; Department of Epidemiology and Public Health, University of Maryland, School of Medicine, 660 West Redwood Street, Baltimore, MD 21201
cadebamowo@som.umaryland.edu

Abstract

Objective: Studies, mainly from high-income countries, suggest that there are ethnic and racial variations in prevalence of uterine fibroids (UF). However, there have been few studies of the epidemiology of UF in Sub-Saharan Africa (SSA). We reviewed published articles on the epidemiology of UF in SSA.

Design: This was a scoping review of literature.

Settings: We searched three databases (PubMed, African Wide Information (EBSCO) and African Journals OnLine (AJOL)). The search for eligible articles was conducted between December 2019 and January 2021.

Primary and secondary outcome measures: To describe the reported prevalence/incidence of, and risk factors for UF in SSA.

Results: Of the 1,052 articles retrieved, 9 met the inclusion criteria for review. The articles were from Nigeria (4/9), Ghana (2/9), Cameroon (1/9), Kenya (1/9), and South Africa (1/9). Two studies from pathology departments and three studies from radiology departments reported prevalence of UF. We did not find any study on the incidence or genomics of UF in SSA. Of the three studies that reported on the risk factors of UF, only one case-control study that was conducted using retrospective data of attendees at a gynaecological clinic conducted multivariable analysis.

Conclusion: There is lack of robust epidemiological studies of the prevalence, incidence, and risk factors of UF in SSA. There is urgent need to study epidemiological and genomics risk factors of UF in SSA because UF is the commonest gynaecological neoplasm in this population where it is associated with significant morbidity and occasional, usually perioperative, mortality.

Keywords: *Uterine fibroids, Leiomyoma, Scoping review, epidemiology, Sub-Saharan Africa (SSA)*

Strengths and Limitations

- We comprehensively reviewed all publications on Uterine Fibroids (UF) in sub-Saharan African (SSA) women, and found dearth of robust epidemiologic studies and no genomic studies despite UF being the commonest neoplasm in this population.
- We were careful to correctly interpret the results of the publications we reviewed
- Because there were so few high quality studies, we were unable to conduct a systematic review and to combine effect estimators to generate summary statistics.
- While unlikely, we may have omitted eligible articles that were not in the three major research databases we searched (PubMed, AWI and AJOL) because many SSA journals are not indexed.
- The interpretation of this review is limited to published information in the manuscript we reviewed, and we assumed that missing information were not collected.

Introduction

Uterine fibroids or uterine leiomyomas (UF) are the commonest neoplasms affecting women.[1] They are typically composed of disordered fascicles of smooth muscle cells, vascular smooth-muscle cells, fibroblasts, leiomyoma-associated fibroblasts, and an excess of acellular extracellular matrix (ECM)[2]. They tend to be multiple and may be found in any part of the uterus however, they are commonest in the muscular wall of the uterus (the myometrium).

The incidence and prevalence of UF reported in the literature varies significantly by study design, methods of diagnosis, ethnic composition and age distribution of study participants.[1,3] The cumulative incidence of UFs by the age of 50 years in women in developed countries is 70 – 80%.[1,4]

Variations in the incidence and prevalence of UF by race and ethnic groups have been widely reported. Studies show that the incidence and prevalence of UF in women of African ancestry is higher than that in other races.[4-6] For example, a large longitudinal study (Nurses' Health Study II) in the USA showed that the incidence of UF confirmed by pelvic examination, ultrasound (USS) or hysterectomy per 1000 woman-years was 37.9 in African American, 14.5 in Hispanic, 12.5 in White and 10.4 in Asian women.[5] In another longitudinal study conducted in United Kingdom, the crude incidence of UF based on primary care physicians' diagnosis with USS, hysteroscopy, laparoscopy or pelvic examination was 5.8 per 1000 woman-years.[7]

There are several epidemiological risk factors for UF. These include advanced age, race, age at menarche, low or nulliparity, family history, obesity, diet, physical activity, smoking, oral contraceptives, hormone replacement therapy, environmental exposure to high levels of estrogen and progesterone, and vitamin D deficiency.[3,8-10] Age is consistently associated with the incidence and prevalence of UF irrespective of ethnicity, race and other risk factors. In general, the risk of UF is about 4-11 times higher in women aged 40-60 years compared to 20-30 years old women and women older than 60 years.[1,3] Several studies show that early age at menarche is associated with higher risk

UF.[3,11,12] Multiparity is linearly associated with reduced risk of UF.[3,13] The risk reduction among multiparous women ranges from 20 to 50% compared to nulliparous women.[1]

Overweight and obesity are independent risk factors for UF.[14] A meta-analysis of 325,899 women among whom 19,593 had UF showed association with obesity.[14] The association was present whether obesity was assessed using waist-to-hip ratio (WHR), waist circumference, weight change from age 18 years, or body mass index (BMI).[14] Some studies found a dose response relationship between obesity and UF while other studies did not find such relationship.[3,14-16]

While few studies reported no associations between dietary intakes and UF, other studies showed a reduced risk with consumption of vegetables and fruits, and increased risk with intakes of food additives, sweeteners, soya milk and dietary fats.[1,14,17-19] Most studies found low level of serum vitamin D to be associated with increased risk of UF while a few reported no effect.[20,21] The association between vitamin D and UF was stronger in black compared to White women. Exposure to sunlight for more than an hour a day was also associated with reduced risk of UF.[20] Smoking was associated with reduced risk of UF, especially in women with low BMI.[1] Most studies reported an inverse relationship between regular physical activities and risk of UF.[3,19] Oral and injectable contraceptives use were associated with reduced risk of UF, however a few studies found increased or no risk in women using oral contraceptives.[1,3] Hormone replacement therapy or exposure to exogenous hormones, particularly among postmenopausal women was associated with increased risk of UF in some studies.[3]

Genetic and epigenetic factors have been associated with risk of UF. Positive family history is associated with increased risk of UF and higher risk was reported among sisters.[1,22-26] The estimates of heritability for UF were 26 to 69% in twin studies while data from GWAS reported heritability risk of 13%.[27,28] The risk of UF is 2.5-fold among first degree relatives compared with the general population.[28] The concordance rate of UF among monozygotic twins is twice that of dizygotic twins of the same sex, and a lot higher than in first-degree relatives.[28,29] Recently, genome wide association studies (GWAS) identified several candidate loci for UF in chromosome regions among African

American - 22q13.1 (*CYTH4*), Caucasian - 11p15.5 (*BETIL*), 17q25.3 (*FASN, CCDC57, and SLC16A3*), 22q13.1 (*TNRC6B*), and Asian - 10q24.33 (*OBFC1*), 11p15.5(*BET1L*), and 22q13.1 (*TNRC6B*) – populations.[30-33]

UF is associated with significant morbidity and substantial socio-economic costs.[34-36] Data from a global systematic review of the cost of UF showed that the total direct and indirect cost after diagnosis or from surgical care ranged from US$11,717 to 25,023 per patient per year.[37] In United States, the annual cost of UF to the economy was estimated to be between US$5.9 to 34.4 billion with obstetric complications contributing the highest fraction of the economic burden.[38]

Consistent with the high incidence and prevalence of UF in African populations in developed countries, case reports and clinical evidence suggest high prevalence of UF in black women living in Africa. However, in contrast to developed countries, there have been very few, adequately powered, systematic epidemiological studies of UF in Africa. In this scoping review of current publications on the epidemiology of UF in Africa, we aim to establish the state of the evidence and their limitations, the burden of UF and priorities for research on UF in black women living in SSA.

Methods

In this review, we used the Joanna Briggs Institute (JBI) guidelines for the conduct of systematic scoping review which was earlier described by Arksey and O'Malley.[39,40] Briefly, we base this review on five frameworks: (a) identifying the research question, (b) identifying the relevant studies (search strategy), (c) selecting the eligible studies, (d) charting the data and (e) collating, summarising, and reporting the results with or without consultation with experts on the specific field. [40]

Research question

The research questions for this scoping review are: What are the prevalence and incidence of UF among black women in SSA? What are the risk factors for UF among SSA women?

Information sources and search strategy

We conducted a systematic search of three online databases for records in English: PubMed, African Wide Information (EBSCO) and African Journal Online (AJOL). We used the following keywords to search the databases to retrieve published articles on the incidence, prevalence, and risk factors of UF; uterine fibroids or fibroids or leiomyoma or myoma; prevalence, incidence, risk factors or causes and Sub-Saharan Africa (SSA) (using sub-regions within SSA (West Africa OR East Africa OR Central Africa OR Southern Africa), and by specific country names) (Supplementary Table 1 – Search Term Strategy). We used Boolean terms AND/OR to separate the keywords during the search. We included Medical Subject Headings (MeSH) terms in the search terms. We also manually searched references and bibliography of relevant articles on this subject. The search was conducted between December 2019 and 27th January 2021.

Eligibility criteria

We used the PICO format (population, intervention, comparator, and outcome) to design the eligibility criteria for the studies that were included in this review. These are (a) published peer reviewed article with observational or experimental design that reported on the aetiology or risk factors or incidence or prevalence or proportion of women with UFs and (b) data must have been collected in SSA among

indigenous black women population. We excluded case reports, letter to editors or expert opinion without primary data on UFs in SSA as well as studies that only reported the outcome of treatment.

Study Selection process

All titles retrieved from searches were compiled and reviewed with Endnote X 8.0 (Thompson Reuters). We removed all duplicates using the Endnote automated system and manually. We screened abstracts in accordance with our inclusion and exclusion criteria. Next, we screened the full texts of abstracts that were eligible for further consideration. Only articles that met the inclusion criteria during full text screening were finally selected for data charting in this review.

Charting data

We entered our data into a prepared Microsoft Excel sheet using the following data charting fields: authors, date, country, study design, aim/objectives, sample size, recruitment strategy (probability or non-probability sampling), study settings (health facility/community/online), outcome measured (prevalence/incidence/proportion), analysis (descriptive/test of association/multivariable analysis) and summary of key findings.

Collating, summarising, and reporting the results

We present a descriptive summary of eligible studies and we created a Prisma-ScR flow chart to summarise the process and number of articles that were finally selected for data charting (Supplementary Table 2).[41] The chart shows the overall number of studies included, study designs and settings, publication years, the characteristics of the study populations, the outcomes reported, and the countries where the studies were conducted. In line with scoping reviews' methodology, we did not perform an assessment of the quality of the included studies.

Patient and Public Involvement

It was not possible to describe patient and public involvement in this research.

Results

We retrieved 1,052 studies from the three databases (Figure 1). After removal of duplicate publications, we screened 484 titles and abstracts and found only 48 articles were eligible for full-text screening. We excluded 39 of the 48 full text articles because 17 of them were on symptoms/management of UF, 7 were animal studies, 5 each were case reports and reviews, 2 were from outside SSA, 1 each were on recurrent UF after treatment, full texts not available and on somatic genetic mutation in UF. Of the 9 studies that met the inclusion criteria, 4 were from Nigeria,[42-45] 2 from Ghana,[46,47] and 1 study each from Cameroon,[48] Kenya[49] and South Africa.[50]

Incidence or prevalence of UF

Five of the 9 studies screened described the prevalence of UF (Table 1).[42,44,46,48,50]

Table 1: Descriptive analysis of studies included in the scoping review

Author; Year	Reference	Research focus	Study design	Sampling methods	Sample size	Outcome measured	Age of study participants	Summary of key findings
Tiltman et. al. 1998 [South Africa]	50	Pathology	Case series	Non-probability	661	Proportion of UF within hysterectomy specimen	12.0-84.0	The proportion of UF was 427/661 (64.6%)
Wango et. al. 2002 [Kenya]	49	Pathology	Case series	Not clearly described	20	Evaluation of estradiol, progesterone, and their receptors	Range 31.0-42.0	The UF tissue contained significantly higher levels of estrogen receptor (28.2±1.6 vs 19.1±0.4 fm/mg protein) and progesterone receptor (16.8±0.7 vs 9.4±0.2 fm/mg protein) compared to normal myometrial tissue, a relatively significant higher levels of estrogen (1117.6±20.9 vs 616.9±19.8 pm/mg protein) and progesterone (7.7±0.25 vs 3.2±0.34 nm/mg protein) in the myometrium than in the leiomyomata.
Mohammed et. al. 2005 [Nigeria]	42	Pathology	Case series	Non-probability	209	Proportion of UF pathological specimen & degenerative changes	Range 25.0-50.0	The proportion of myometrial UF was 2.2% of all surgical specimen over five years.
Eze et. al. 2013 [Nigeria]	43	Radiology	Case control	Non-probability	200 (100 cases vs 100 controls)	Frequency and growth rate of uterine fibroids in pregnancy	Cases (31.6 ± 4.5yr); Controls (29.1 ± 5.5yr)	The frequency of UFs in pregnancy was 12.3%; the commonest type was subserous fibroids (27.5%). The mean size of UFs measured on ultrasound was lowest during third scan.
Oluwole et. al. 2015 [Nigeria]	44	Clinical	Case control	Non-probability	580	Proportion of UF & risk factor analysis	35.5±5.8	The proportion of women with UFs was 31% (178/580). Presence of UFs was associated with 40-49years (OR=4.9%; 95%CI 1.8-31.1); lower parity (OR=0.6; 95%CI 0.2-0.9); family history of UFs (OR=1.9; 95%CI 1.9-4.8); and history of infertility (OR=5.0; 95%CI 0.9-25.9)
Awowole et. al. 2016 [Nigeria]	45	Pathology	Cross-sectional	Non-probability	60	To measure expression of estrogen receptor α (ERα) and progesterone receptor (PR) in myometrium and UF	26.0-53.0	UF had a higher mean expression of estrogen receptor (Erα) (H-score 193.4 ± 64.6 vs 153.3 ± 69.1; p = 0.01) and progesterone receptor (PR) (214.9 ± 66.6 vs 171.5 ± 63.5; p < 0.001) than in myometrial tissues. The tumor diameter correlated negatively with the immunoscores of both receptors irrespective of age, parity, and body mass index, but this was only significant for PR (p = –0.44; p<0.001).
Sarkodie et. al. 2016a [Ghana]	46	Radiology	Cross-sectional	Non-probability	244	Prevalence of UF & risk factors analysis	14.0-54.0	In this study, 23 % (38/168) of women <35 had prevalent fibroids, compared to 67 % (36/54) of

								women 35–44, and 73 % (16/22) of women at 45 or above years. Factors that associated significantly with UF in Ghanaian women included obesity (X2 = 17.3, p-value = 0.001), participant's age range (X2 = 47.4, p = 0.001), parity (X2 = −10.2, p = 0.001), and age at last delivery (X2 = 34.6, p = 0.001).
Sarkodie et. al. 2016b [Ghana]	47	Radiology	Cross-sectional	Non-probability	244	Assessment of sonographic characteristics of UF	14.0-54.0	The prevalence of UF was 36.9 % (90/244). The majority of the UFs were intramural (57.8 %) with only 4.4 % noted as sub-mucosal. Most (55.6 %) of the UFs were located in more than one part of the uterus.
Egbe et. al. 2018 [Cameroon]	48	Radiology & Clinical	Cross-sectional	Non-probability	226	Proportion of UF & risk factors analysis	≥21.0	The prevalence of UF in pregnancy was 16.7% (38/226). Respondents with UF were older than those without (p < 0.001) and of low parity (p = 0.02).

UF – Uterine Fibroids; CI – Confidence interval; OR – Odds ratio

Two of these studies, one each from pathology departments in single institutions in South Africa and Nigeria, examined the proportion of UF in surgical specimens.[42,50] In Northern Nigeria, UF accounted for 2.2% of all surgical specimen at a single facility over a five-year period.[42] The South African study reported that the proportion of UF among all hysterectomy specimens in a single institution over a six-month period was 64.6%.[50]

A cross-sectional study of pregnant women undergoing abdominal USS examination in two regional hospitals in Cameroun reported that 16.8% (38/226) had UF.[48] Another cross-sectional study in Ghana among 244 non-pregnant women referred for abdominal USS showed that 36.9% had UF and the proportion of women with UF increased with age.[46] A 2-year retrospective review of attendees at the gynaecology clinic of a public tertiary health institution in Nigeria showed that 30.7% (178/580) of all patients had a diagnosis of UF.[44] Another study of pregnant women referred for prenatal abdominal USS at a tertiary hospital in eastern Nigeria showed that the prevalence of UF was 12.3% during pregnancy.[43]

Role of Oestrogen, Progesterone, and their receptors

A study in Kenya reported on cytosolic quantification of oestrogen and progesterone and their receptors in UF tissue measured using radioimmunoassay.[49] The study showed that UF contained lower levels of oestrogen and progesterone but higher levels of receptors for these hormones compared to normal uterine tissue.[49] In a more recent Nigerian study using immunohistochemistry, the level of oestrogen and progesterone receptors in UF was higher than in uterine tissue.[45] The Nigerian study further showed a significant negative correlation between UF size and the progesterone receptors levels only (Table 1).[45]

Risk factors for UF

Three studies presented data on risk factors of UF (Tables 1 and 2).[44,46,48]

Table 2: Summary of reported risk factors associated with UF in SSA

Risk factors	Pregnant women		Non-Pregnant women
	Egbe et. al. 2018 [Cross-sectional study from Cameroon]	**Sarkodie et. al. 2016a [Cross-sectional study from Ghana]**	**Oluwole et. al. 2015 [Case control study from Nigeria]**
Advanced age	↑	↑	↑
Family history	Not considered	Not considered	↑
Obesity	Not considered	↑	↓
Nulliparity	Not considered	↑	Not considered
Gravidity	↑	Not considered	Not considered
Advanced age at delivery	Not considered	↑	Not considered
At least primiparity	Not considered	Not considered	↓

↑ - Increased risk, ↓ - Decreased risk, Not considered as a risk factor in the study

In a Nigerian case-control study of gynaecology clinic attendees, advanced age (OR=4.90; 95%CI 1.80-31.1) and positive family history (OR=3.0; 95%CI 1.90-4.80) were associated with higher risk while obesity (OR=0.4; 95%CI 0.10-0.90) and primiparity (OR=0.60; 95%CI 0.20-0.90) were associated with lower risk of UF.[44] A cross-sectional study of 244 women referred for abdominal USS at three centres in Ghana found that women with UF tended to be older (p=0.001), obese (0.001), older at last pregnancy and delivery (p=0.001) and have lower parity (p=0.001). [46] In another cross-sectional study of factors associated with UF in pregnancy in Cameroun, women with UF were older (p<0.001) and had higher gravidity (p=0.02). [48]

Discussion

In this review, we mapped published epidemiological studies on incidence, prevalence, and risk factors for UF in indigenous African women. Our results confirmed the paucity of systematic epidemiological study of UF among black women in Africa. Only few studies have some information on prevalence/proportion of, and risk factors for UF.[42,44,46,48,50] The five studies that reported the prevalence of UF used different populations, denominators, and study designs.[42,44,46,48,50] Two studies from pathology departments in Nigeria and South Africa used different reporting periods and denominators to calculate the proportions of UF.[42,50] We also observed variations in the reporting of the prevalence of UF in pregnancy in the two studies from radiology departments in Nigeria and Cameroon.[43,48] They both used convenience sampling technique and were silent on the gestational ages of participants. The only Nigerian study that presented data on the prevalence of UF among non-pregnant women was a retrospective review of case records that used all other attendees at a gynaecological clinic as controls.[44] There was no study in this review that has information on the incidence of UF in pregnant or non-pregnant women.

Two studies were on the role of oestrogen and progesterone and their receptors. The two hormonal studies used different diagnostic techniques (radioimmunoassay versus immunochemistry), laboratory

estimation of cut-off levels for oestrogen and progesterone and comparator groups (UF and normal myometrial tissue from same patient versus UF and normal myometrial tissue from different patients as cases and control).[45,49] The observed differences in the methodology of the two studies make it difficult to compare and interpret their findings. We observed that the sample sizes of these three studies were too small to allow for rigorous multivariable analysis for confounders. In addition, the three studies were conducted with specimen from women who had treatment in specific health facilities.

Three studies described risk factors for UF among black African women, but they all used different research designs and data analysis techniques.[44,46,48] All the studies were conducted within single facilities, two were cross-sectional and one was a retrospective case control study. The risk factors identified in the three studies were similar to those reported in studies conducted in USA, Europe and Asia. [5,12,51] Briefly, advancing age was the only risk factors that was common to all three studies and low parity was reported in two studies.[44,46,48] The only other risk factor reported among non-pregnant women was self-report of family history of UF.[44] Obesity was reported as a protective factor in non-pregnant Nigerian women and as a risk factor in pregnant women in Ghana.[44,48] The tests for association in these studies were not well described in the methods sections of their manuscripts.[44,46,48] The studies from Cameroon and Ghana used bivariate tests and did not adjust for age in their analyses.[46,48] The only Nigerian study that used multivariable analysis to adjust for confounders, used data collected from a retrospective review of cases managed in a tertiary public health facility and assigned other attendees as controls.[44]

Although, we did not assess the risk of bias in studies that we reviewed because that is outside the objective of scoping review generally, we observed that the majority of the studies used data collected from case series or cross-sectional studies (6/9) while two (3/9) were case control studies.[42-50] None of the 9 studies we reviewed used probability sampling technique to select their subjects and only one study reported on sample size and power calculation.

We found several gaps in the epidemiology of UF in SSA. There was no genomic epidemiology study of uterine fibroid in SSA. Studies from high income countries have shown that only 20.0-40.0% of women with symptomatic UF seek medical treatment, suggesting that a significant number of women with UF are not captured by facilities based studies.[52] We did not find any published population based study with adequate statistical power and sampling strategy which can generate generalizable information on incidence, prevalence and risk factors of UF among indigenous black African women. There are many epidemiological risk factors of UF that are yet to be investigated in SSA. These factors include reproductive factors (age at menarche and menopause, birth interval or inter pregnancy interval, contraceptives, and hormone replacement therapy), diets including vitamin D, trace elements and heavy metals, lifestyle and physical activity, reproductive tract infections, microbiome, and pollution. [3,8,12,53,54] Lack of information on these risk factors prevent development of preventive and therapeutic interventions. This is a serious gap in knowledge considering the morbidity, mortality, and economic costs of UF in SSA.

The interpretation of findings from this scoping review may be limited for the following reasons. We searched published articles from online databases only. We may have missed papers published in journals that are not indexed in these online databases. We excluded one article that we could not retrieve the full texts, but the abstract shows that this was on the association between UF and BMI. Despite these limitations, this scoping review confirmed the dearth of studies on the epidemiology of UF among SSA women and argues for urgent remediation of this situation.

Conclusions

Our results show that there is limited information on the epidemiology of UF and identified gaps in knowledge of UF among women in SSA despite its high prevalence, morbidity, and economic costs. We recommend urgent implementation of well-designed and adequately powered studies to address this gap.

Authors' contribution: CAA conceived and designed the study. He conducted literature review, reviewed, revised, and approved the manuscript. IMB participated in the design, conducted literature search, screening of articles and data charting. He wrote the first draft, revised, and approved the manuscript.

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Patient consent for publication: Not required.

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Data availability statement: The data will be made available upon request from the corresponding author.

References:

1. Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. *BJOG* 2017; **124**(10): 1501-12.

2. Holdsworth-Carson SJ, Zaitseva M, Vollenhoven BJ, Rogers PA. Clonality of smooth muscle and fibroblast cell populations isolated from human fibroid and myometrial tissues. *Molecular human reproduction* 2014; **20**(3): 250-9.

3. Wise LA, Laughlin-Tommaso SK. Epidemiology of Uterine Fibroids: From Menarche to Menopause. *Clin Obstet Gynecol* 2016; **59**(1): 2-24.

4. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol* 2003; **188**(1): 100-7.

5. Marshall LM, Spiegelman D, Barbieri RL, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstet Gynecol* 1997; **90**(6): 967-73.

6. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Age-specific incidence rates for self-reported uterine leiomyomata in the Black Women's Health Study. *Obstet Gynecol* 2005; **105**(3): 563-8.

7. Martin-Merino E, Wallander MA, Andersson S, Soriano-Gabarro M, Rodriguez LA. The reporting and diagnosis of uterine fibroids in the UK: an observational study. *BMC Womens Health* 2016; **16**: 45.

8. Brakta S, Diamond JS, Al-Hendy A, Diamond MP, Halder SK. Role of vitamin D in uterine fibroid biology. *Fertil Steril* 2015; **104**(3): 698-706.

9. Baird DD, Harmon QE, Upson K, et al. A Prospective, Ultrasound-Based Study to Evaluate Risk Factors for Uterine Fibroid Incidence and Growth: Methods and Results of Recruitment. *Journal of women's health* 2015; **24**(11): 907-15.

10. Wise LA, Palmer JR, Rosenberg L, Haddad SA, Ruiz-Narvaez EA. FASN, dietary fat intake, and risk of uterine leiomyomata in the Black Women's Health Study. *Fertil Steril* 2016; **106**(5): 1136-41.

11. Styer AK, Rueda BR. The Epidemiology and Genetics of Uterine Leiomyoma. *Best practice & research Clinical obstetrics & gynaecology* 2016; **34**: 3-12.

12. Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. *Int J Fertil Steril* 2016; **9**(4): 424-35.

13. Baird DD, Dunson DB. Why is parity protective for uterine fibroids? *Epidemiology* 2003; **14**(2): 247-50.

14. Qin H, Lin Z, Vásquez E, Luan X, Guo F, Xu L. Association between obesity and the risk of uterine fibroids: a systematic review and meta-analysis. *J Epidemiol Community Health* 2021; **75**(2): 197-204.

15. Lee JE, Song S, Cho E, et al. Weight change and risk of uterine leiomyomas: Korea Nurses' Health Study. *Curr Med Res Opin* 2018; **34**(11): 1913-9.

16. Sato F, Nishi M, Kudo R, Miyake H. Body fat distribution and uterine leiomyomas. *J Epidemiol* 1998; **8**(3): 176-80.

17. Shen Y, Xu Q, Xu J, Ren ML, Cai YL. Environmental exposure and risk of uterine leiomyoma: an epidemiologic survey. *Eur Rev Med Pharmacol Sci* 2013; **17**(23): 3249-56.

18. Wise LA, Radin RG, Kumanyika SK, Ruiz-Narvaez EA, Palmer JR, Rosenberg L. Prospective study of dietary fat and risk of uterine leiomyomata. *Am J Clin Nutr* 2014; **99**(5): 1105-16.

19. He Y, Zeng Q, Dong S, Qin L, Li G, Wang P. Associations between uterine fibroids and lifestyles including diet, physical activity and stress: a case-control study in China. *Asia Pac J Clin Nutr* 2013; **22**(1): 109-17.

20. Baird DD, Hill MC, Schectman JM, Hollis BW. Vitamin d and the risk of uterine fibroids. *Epidemiology* 2013; **24**(3): 447-53.

21. Ciebiera M, Włodarczyk M, Ciebiera M, Zaręba K, Łukaszuk K, Jakiel G. Vitamin D and uterine fibroids—review of the literature and novel concepts. *International journal of molecular sciences* 2018; **19**(7): 2051.

22. D'Aloisio AA, Baird DD, DeRoo LA, Sandler DP. Early-life exposures and early-onset uterine leiomyomata in black women in the Sister Study. *Environ Health Perspect* 2012; **120**(3): 406-12.

23. Mu X, Du X, Yao K, et al. Association between HSD17B1 rs605059 polymorphisms and the risk of uterine diseases: a systemic review and meta-analysis. *International journal of clinical and experimental pathology* 2015; **8**(6): 6012-8.

24. Bideau VS, Alleyne AT. Leu/Val SNP polymorphism of CYP1B1 and risk of uterine leiomyoma in a Black population. *Tumour Biol* 2016; **37**(3): 4035-40.

25. Gallagher CS, Morton CC. Genetic Association Studies in Uterine Fibroids: Risk Alleles Presage the Path to Personalized Therapies. *Seminars in reproductive medicine* 2016; **34**(4): 235-41.

26. Aissani B, Zhang K, Wiener H. Genetic determinants of uterine fibroid size in the multiethnic NIEHS uterine fibroid study. *Int J Mol Epidemiol Genet* 2015; **6**(1): 9-19.

27. Ponomarenko I, Reshetnikov E, Polonikov A, et al. Candidate Genes for Age at Menarche Are Associated With Uterine Leiomyoma. *Front Genet* 2020; **11**: 512940.

28. Luoto R, Kaprio J, Rutanen EM, Taipale P, Perola M, Koskenvuo M. Heritability and risk factors of uterine fibroids--the Finnish Twin Cohort study. *Maturitas* 2000; **37**(1): 15-26.

29. Vikhlyaeva EM, Khodzhaeva ZS, Fantschenko ND. Familial predisposition to uterine leiomyomas. *Int J Gynaecol Obstet* 1995; **51**(2): 127-31.

30. Hellwege JN, Jeff JM, Wise LA, et al. A multi-stage genome-wide association study of uterine fibroids in African Americans. *Hum Genet* 2017; **136**(10): 1363-73.

31. Edwards TL, Michels KA, Hartmann KE, Velez Edwards DR. BET1L and TNRC6B associate with uterine fibroid risk among European Americans. *Hum Genet* 2013; **132**(8): 943-53.

32. Cha P-C, Takahashi A, Hosono N, et al. A genome-wide association study identifies three loci associated with susceptibility to uterine fibroids. *Nature genetics* 2011; **43**(5): 447-50.

33. Eggert SL, Huyck KL, Somasundaram P, et al. Genome-wide linkage and association analyses implicate FASN in predisposition to uterine leiomyomata. *The American Journal of Human Genetics* 2012; **91**(4): 621-8.

34. Agboola AD, Bello OO, Olayemi OO. A clinical audit of the patterns of presentations and complications of abdominal myomectomy at the University College Hospital, Ibadan, Nigeria. *J Obstet Gynaecol* 2021: 1-6.

35. Yorgancı A, Meydanlı MM, Kadıoğlu N, et al. Incidence and outcome of occult uterine sarcoma: A multi-centre study of 18604 operations performed for presumed uterine leiomyoma. *J Gynecol Obstet Hum Reprod* 2020; **49**(1): 101631.

36. Foth D, Rohl FW, Friedrich C, et al. Symptoms of uterine myomas: data of an epidemiological study in Germany. *Arch Gynecol Obstet* 2017; **295**(2): 415-26.

37. Soliman AM, Yang H, Du EX, Kelkar SS, Winkel C. The direct and indirect costs of uterine fibroid tumors: a systematic review of the literature between 2000 and 2013. *American journal of obstetrics and gynecology* 2015; **213**(2): 141-60.

38. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol* 2012; **206**(3): 211 e1-9.

39. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis, JBI, 2020. Available from https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-20-12. 2020.

40. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International journal of social research methodology* 2005; **8**(1): 19-32.

41. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of Internal Medicine* 2018; **169**(7): 467-73.

42. Mohammed A, Shehu S, Ahmed S, et al. Uterine leiomyomata: a five year clinicopathological review in Zaria, Nigeria. *Nigerian Journal of surgical research* 2005; **7**(1): 206-8.

43. Eze CU, Odumeru E, Ochie K, Nwadike U, Agwuna K. Sonographic assessment of pregnancy co-existing with uterine leiomyoma in Owerri, Nigeria. *African Health Sciences* 2013; **13**(2): 453-60.

44. Oluwole A, Owie E, Babah O, Afolabi B, Oye-Adeniran B. Epidemiology of Uterine Leiomyomata at the Lagos University Teaching Hospital, Idi-Araba, Lagos. *Nigerian Hospital Practice* 2015; **15**(1-3): 14-20.

45. Awowole IO, Makinde ON, Badejoko OO, et al. Clinical correlates of leiomyoma estrogen and progesterone receptors among Nigerian women. *International Journal of Gynecology & Obstetrics* 2016; **135**(3): 314-8.

46. Sarkodie BD, Botwe BO, Adjei DN, Ofori E. Factors associated with uterine fibroid in Ghanaian women undergoing pelvic scans with suspected uterine fibroid. *Fertility research and practice* 2016a; **2**(1): 1-7.

47. Sarkodie BD, Botwe BO, Ofori EK. Uterine fibroid characteristics and sonographic pattern among Ghanaian females undergoing pelvic ultrasound scan: a study at 3-major centres. *BMC women's health* 2016b; **16**(1): 1-6.

48. Egbe TO, Badjang TG, Tchounzou R, Egbe E-N, Ngowe MN. Uterine fibroids in pregnancy: prevalence, clinical presentation, associated factors and outcomes at the Limbe and Buea Regional Hospitals, Cameroon: a cross-sectional study. *BMC research notes* 2018; **11**(1): 1-6.

49. Wango EO, Tabifor HN, Muchiri LW, Sekadde-Kigondu C, Makawiti DW. Progesterone, estradiol and their receptors in leiomyomata and the adjacent normal myometria of black Kenyan women. *African journal of health sciences* 2002; **9**(2): 123-8.

50. Tiltman AJ. Leiomyomas of the uterine cervix: a study of frequency. *International journal of gynecological pathology: official journal of the International Society of Gynecological Pathologists* 1998; **17**(3): 231-4.

51. Wise LA, Palmer JR, Harlow BL, et al. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African-American women: a prospective study. *Am J Epidemiol* 2004; **159**(2): 113-23.

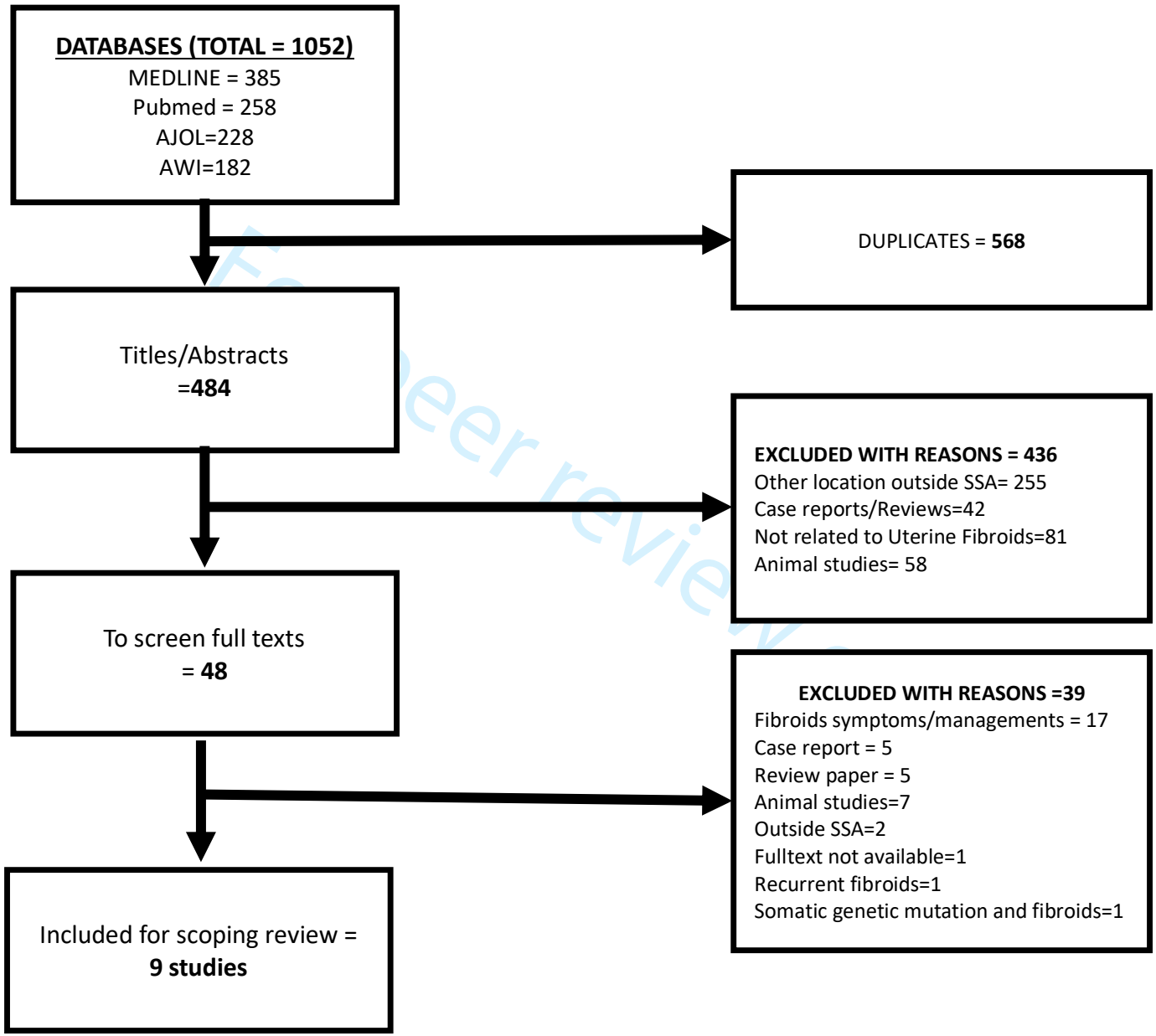
52. Marsh EE, Ekpo GE, Cardozo ER, Brocks M, Dune T, Cohen LS. Racial differences in fibroid prevalence and ultrasound findings in asymptomatic young women (18-30 years old): a pilot study. *Fertil Steril* 2013; **99**(7): 1951-7.

53. Hansen JG, Tang W, Hootman KC, et al. Genetic and environmental factors are associated with serum 25-hydroxyvitamin D concentrations in older African Americans. *J Nutr* 2015; **145**(4): 799-805.

54. Moore KR, Cole SR, Dittmer DP, Schoenbach VJ, Smith JS, Baird DD. Self-Reported Reproductive Tract Infections and Ultrasound Diagnosed Uterine Fibroids in African-American Women. *Journal of women's health* 2015; **24**(6): 489-95.

Figure 1: The Prisma Flow Chart for the scoping review

Figure 1: The Prisma Flow Chart



Supplementary Table 1: Search Strategy used for PubMED

CONCEPTS	SN	TERMS	SEARCH DETAILS
Concept 1: Uterine fibroids	#1	uterine fibroids	"leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR ("uterine"[All Fields] AND "fibroids"[All Fields]) OR "uterine fibroids"[All Fields] OR ("fibroid s"[All Fields] OR "leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "fibroid"[All Fields] OR "fibroids"[All Fields])
	#2	fibroids	fibroids"[All Fields] OR "leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "fibroid"[All Fields] OR "fibroids"[All Fields]
	#3	leiomyoma	leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "leiomyomas"[All Fields] OR "myoma"[MeSH Terms] OR "myoma"[All Fields] OR "myomas"[All Fields] OR "myoma s"[All Fields]
	#4	myoma	"leiomyoma"[MeSH Terms] OR "leiomyoma"[All Fields] OR "leiomyomas"[All Fields] OR "myoma"[MeSH Terms] OR "myoma"[All Fields] OR "myomas"[All Fields] OR "myoma s"[All Fields]
	#5	**#1 OR #2 OR #3 OR #4**	
Concept 2: Epidemiological indicators/measure used	#6	Cause OR causes	"causative"[All Fields] OR "causatively"[All Fields] OR "causatives"[All Fields] OR "cause"[All Fields] OR "caused"[All Fields] OR "causing"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causes"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields] OR "causative"[All Fields] OR "causatively"[All Fields] OR "causatives"[All Fields] OR "cause"[All Fields] OR "caused"[All Fields] OR "causing"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causes"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields]
	#7	aetiology OR etiology	"aetiologie"[All Fields] OR "aetiologies"[All Fields] OR "aetiology"[All Fields] OR "etiologies"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields] OR "aetiologie"[All Fields] OR "aetiologies"[All Fields] OR "aetiology"[All Fields] OR "etiologies"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields]
	#8	Risk factor	"risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk factors"[All Fields] OR ("risk"[All Fields] AND "factor"[All Fields]) OR "risk factor"[All Fields]
	#9	Prevalence OR prevalen*	"epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields]
	#10	Incidence OR inciden*	"epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "incidence"[All Fields] OR "incidence"[MeSH Terms] OR "incidences"[All Fields] OR "incident"[All Fields] OR "incidents"[All Fields]
	#11	epidemiology	"epidemiologies"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "epidemiology"[MeSH Terms] OR "epidemiology s"[All Fields]
	#12	**#6 OR #7 OR #8 OR #9 OR #10 OR #11**	
Concept 3: Women	#13	Women OR Woman	"womans"[All Fields] OR "women"[MeSH Terms] OR "women"[All Fields] OR "woman"[All Fields] OR "women s"[All Fields] OR "womens"[All Fields]
	#14	**#13**	
Concept 4: Sub-Saharan Africa	#15	Africa	"africa"[MeSH Terms] OR "africa"[All Fields] OR "africa s"[All Fields] OR "africas"[All Fields]
	#16	West Africa	"africa, western"[MeSH Terms] OR ("africa"[All Fields] AND "western"[All Fields]) OR "western africa"[All Fields] OR ("west"[All Fields] AND "africa"[All Fields]) OR "west africa"[All Fields]
	#17	East Africa	"africa, eastern"[MeSH Terms] OR ("africa"[All Fields] AND "eastern"[All Fields]) OR "eastern africa"[All Fields] OR ("east"[All Fields] AND "africa"[All Fields]) OR "east africa"[All Fields]
	#18	Central Africa	"africa, central"[MeSH Terms] OR ("africa"[All Fields] AND "central"[All Fields]) OR "central africa"[All Fields] OR ("central"[All Fields] AND "africa"[All Fields])
	#19	Southern Africa	"africa, southern"[MeSH Terms] OR ("africa"[All Fields] AND "southern"[All Fields]) OR "southern africa"[All Fields] OR ("southern"[All Fields] AND "africa"[All Fields])
	#20	Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cameroon OR Cape Verde OR Central	"angola"[MeSH Terms] OR "angola"[All Fields] OR "angola s"[All Fields] OR ("benin"[MeSH Terms] OR "benin"[All Fields] OR "benin s"[All Fields]) OR ("botswana"[MeSH Terms] OR "botswana"[All Fields] OR "botswana s"[All Fields]) OR ("burkina faso"[MeSH Terms] OR ("burkina"[All Fields] AND

		African Republic OR Chad OR Comoros OR Côte d'Ivoire OR Democratic Republic of the Congo OR Djibouti OR Equatorial Guinea Eritrea OR Ethiopia OR Gabon OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Republic of the Congo OR Rwanda OR São Tomé and Príncipe OR Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR South Sudan OR Swaziland OR Tanzania OR The Gambia OR Togo OR Uganda OR Zambia OR Zimbabwe	"faso"[All Fields]) OR "burkina faso"[All Fields]) OR ("burundi"[MeSH Terms] OR "burundi"[All Fields]) OR ("cameroon"[MeSH Terms] OR "cameroon"[All Fields] OR "cameroons"[All Fields] OR "cameroon s"[All Fields]) OR ("cabo verde"[MeSH Terms] OR ("cabo"[All Fields] AND "verde"[All Fields]) OR "cabo verde"[All Fields] OR ("cape"[All Fields] AND "verde"[All Fields]) OR "cape verde"[All Fields]) OR ("central african republic"[MeSH Terms] OR ("central"[All Fields] AND "african"[All Fields] AND "republic"[All Fields]) OR "central african republic"[All Fields]) OR ("chad"[MeSH Terms] OR "chad"[All Fields]) OR ("comoros"[MeSH Terms] OR "comoros"[All Fields] OR "comoro"[All Fields]) OR ("cote d ivoire"[MeSH Terms] OR ("cote"[All Fields] AND "d ivoire"[All Fields]) OR "cote d ivoire"[All Fields]) OR ("democratic republic of the congo"[MeSH Terms] OR ("democratic"[All Fields] AND "republic"[All Fields] AND "congo"[All Fields]) OR "democratic republic of the congo"[All Fields]) OR ("djibouti"[MeSH Terms] OR "djibouti"[All Fields]) OR (("equatorial guinea"[MeSH Terms] OR ("equatorial"[All Fields] AND "guinea"[All Fields]) OR "equatorial guinea"[All Fields]) AND ("eritrea"[MeSH Terms] OR "eritrea"[All Fields])) OR ("ethiopia"[MeSH Terms] OR "ethiopia"[All Fields] OR "ethiopia s"[All Fields]) OR ("gabon"[MeSH Terms] OR "gabon"[All Fields]) OR ("ghana"[MeSH Terms] OR "ghana"[All Fields] OR "ghana s"[All Fields]) OR ("guinea"[MeSH Terms] OR "guinea"[All Fields] OR "guinea s"[All Fields] OR "guineas"[All Fields]) OR ("guinea bissau"[MeSH Terms] OR "guinea bissau"[All Fields] OR ("guinea"[All Fields] AND "bissau"[All Fields]) OR "guinea bissau"[All Fields]) OR ("kenya"[MeSH Terms] OR "kenya"[All Fields] OR "kenya s"[All Fields]) OR ("lesotho"[MeSH Terms] OR "lesotho"[All Fields]) OR ("liberia"[MeSH Terms] OR "liberia"[All Fields] OR "liberia s"[All Fields]) OR ("madagascar"[MeSH Terms] OR "madagascar"[All Fields] OR "madagascar s"[All Fields]) OR ("malawi"[MeSH Terms] OR "malawi"[All Fields] OR "malawi s"[All Fields]) OR ("mali"[MeSH Terms] OR "mali"[All Fields]) OR ("mauritania"[MeSH Terms] OR "mauritania"[All Fields]) OR ("mauritius"[MeSH Terms] OR "mauritius"[All Fields]) OR ("mozambique"[MeSH Terms] OR "mozambique"[All Fields] OR "mozambique s"[All Fields]) OR ("namibia"[MeSH Terms] OR "namibia"[All Fields]) OR ("niger"[MeSH Terms] OR "niger"[All Fields]) OR ("nigeria"[MeSH Terms] OR "nigeria"[All Fields] OR "nigeria s"[All Fields]) OR ("congo"[MeSH Terms] OR "congo"[All Fields] OR ("republic"[All Fields] AND "congo"[All Fields]) OR "republic of the congo"[All Fields]) OR ("rwanda"[MeSH Terms] OR "rwanda"[All Fields] OR "rwanda s"[All Fields]) OR ("sao tome and principe"[MeSH Terms] OR ("sao"[All Fields] AND "tome"[All Fields] AND "principe"[All Fields]) OR "sao tome and principe"[All Fields]) OR ("senegal"[MeSH Terms] OR "senegal"[All Fields] OR "senegal s"[All Fields]) OR ("seychelles"[MeSH Terms] OR "seychelles"[All Fields]) OR ("sierra leone"[MeSH Terms] OR ("sierra"[All Fields] AND "leone"[All Fields]) OR "sierra leone"[All Fields]) OR ("somalia"[MeSH Terms] OR "somalia"[All Fields]) OR ("south africa"[MeSH Terms] OR ("south"[All Fields] AND "africa"[All Fields]) OR "south africa"[All Fields]) OR ("south sudan"[MeSH Terms] OR ("south"[All Fields] AND "sudan"[All Fields]) OR "south sudan"[All Fields]) OR ("eswatini"[MeSH Terms] OR "eswatini"[All Fields] OR "swaziland"[All Fields]) OR ("tanzania"[MeSH Terms] OR "tanzania"[All Fields] OR "tanzania s"[All Fields]) OR ("gambia"[MeSH Terms] OR "gambia"[All Fields] OR "the gambia"[All Fields]) OR ("togo"[MeSH Terms] OR "togo"[All Fields]) OR ("uganda"[MeSH Terms] OR "uganda"[All Fields] OR "uganda s"[All Fields]) OR ("zambia"[MeSH Terms] OR "zambia"[All Fields] OR "zambia s"[All Fields]) OR ("zimbabwe"[MeSH Terms] OR "zimbabwe"[All Fields] OR "zimbabwe s"[All Fields])
	#21	**#15 OR #16 OR #17 OR #18 OR #19 OR #20**	
Final Combined Terms	**#23**	**#5 AND #12 AND #14 AND #21**	

These search terms were used in the 3 databases (MEDLINE/PubMed, AJOL &AWI)

Supplementary Table 2: Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	#1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	#2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	#3, 4, & 5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	#6 & 7
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	Not done
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	#7 & 8
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	#7
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	# 7 [Supplement Table 2]
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	#8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	#8
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	#8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	#8
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	#8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	#9
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	#9 & 10
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	#9 & 10
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	#9 & 10
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	#9 & 10
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	#11, 12 & 13

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Limitations	20	Discuss the limitations of the scoping review process.	#13
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	#13
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	#14

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.
* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.
† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).
‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.