

Supplementary File S1

Search Strategy for the study entitled “Pathophysiological Consequences Associated with Hormonal Contraceptives in Sub-Saharan Africa: A Scoping Review”

This document outlines the comprehensive search strategies employed to identify relevant studies for the scoping review from PubMed, Wiley Online Library, Africa Journal Online (AJOL), and grey literature via Google Scholar. The search was conducted between January 2000 and July 2025, focusing on English publications.

PubMed Search Strategy

- **Database:** PubMed
- **Date Range:** January 2000 – July 2025
- **Languages:** English
- **Search String:**
 - ("hormonal contraceptives" OR "combined oral contraceptives" OR "progestin-only pills" OR "depot medroxyprogesterone acetate" OR "norethisterone enanthate" OR "subdermal implants" OR "hormonal IUD" OR "contraceptive methods") AND ("Sub-Saharan Africa" OR "SSA" OR specific country names [e.g., Nigeria, Kenya, South Africa]) AND ("pathophysiology" OR "physiological changes" OR "anemia" OR "cardiometabolic risk" OR "lipid profile" OR "blood pressure" OR "glucose metabolism" OR "bone mineral density" OR "immune response" OR "HIV acquisition" OR "menstrual irregularities")
- **Filters:** Humans, Female, Male, 15-49 years
- **Additional Steps:** MeSH terms ("Contraceptives, Hormonal"[Mesh], "Africa South of the Sahara"[Mesh]) were exploded and combined with keywords using Boolean operators (AND, OR). Results were limited to peer-reviewed articles.

Wiley Online Library Search Strategy

- **Database:** Wiley Online Library
- **Date Range:** January 2000 – July 2025
- **Languages:** English
- **Search String:**
 - ("hormonal contraceptives" OR "combined oral contraceptives" OR "progestin-only pills" OR "DMPA" OR "NET-EN" OR "implants" OR "hormonal IUD") AND ("Sub-Saharan Africa" OR "SSA" OR "Nigeria" OR "Kenya" OR "South Africa") AND ("pathophysiological effects" OR "anemia" OR "metabolic changes" OR "cardiovascular

risk" OR "lipids" OR "insulin resistance" OR "bone health" OR "immune function" OR "HIV risk")

- **Filters:** Publication years 2000-2025, peer-reviewed articles, subject areas (Medicine, Public Health)
- **Additional Steps:** Advanced search options were used to combine terms with Boolean operators. Results were manually screened for relevance.

Africa Journal Online (AJOL) Search Strategy

- **Database:** Africa Journal Online (AJOL)
- **Date Range:** January 2000 – July 2025
- **Languages:** English
- **Search String:**
 - ("hormonal contraception" OR "oral contraceptives" OR "injectable contraceptives" OR "implants" OR "IUD") AND ("Sub-Saharan Africa" OR "SSA" OR country-specific terms) AND ("physiological impact" OR "anemia" OR "cardiometabolic outcomes" OR "lipid levels" OR "blood pressure" OR "bone density" OR "immune response" OR "HIV transmission")
- **Filters:** Open-access and subscription-based journals, publication years 2000-2025
- **Additional Steps:** Manual keyword searches were conducted due to limited advanced search functionality, with results cross-checked against inclusion criteria.

Grey Literature Search Strategy (Google Scholar)

- **Source:** Google Scholar
- **Date Range:** January 2000 – July 2025
- **Languages:** English, French, Portuguese
- **Search String:**
 - ("hormonal contraceptives" "Sub-Saharan Africa" "pathophysiology" OR "anemia" OR "cardiometabolic" OR "lipids" OR "immune" OR "HIV"
- **Filters:** Publication years 2000-2025, sorted by relevance
- **Notes:** Exclusions applied to commercial sites and login-required pages to prioritize open-access grey literature.

General Notes

- Boolean operators (AND, OR) were used to combine terms, with truncation () *applied where applicable (e.g., "contracept")*.
- Search results were deduplicated using reference management software and screened by two independent reviewers.

Supplementary file S2:

Table S1: Data extraction sheet for the study entitled “Pathophysiological Consequences Associated with Hormonal Contraceptives in Sub-Saharan Africa: A Scoping Review”

Serial No	First Author (Year)	Study Country	Study Design	Sample Size	Contraceptive Methods Used	Pathologies/ Outcomes Measured	Key Results (Effect Sizes, 95% CI, p-values)	Limitations
1	(Chung et al., 2025)	Multi-SSA (46 countries)	Cross-sectional (DHS)	790,065	Hormonal (pills, injectables, implants)	Anemia (Hb <12 g/dL)	AOR=0.73 (0.65–0.83, p<0.001); injectables AOR=0.64 (0.55–0.74, p<0.001); pills AOR=0.78 (0.68–0.90, p<0.001); implants AOR=0.83 (0.71–0.97, p=0.019)	Cross-sectional design limits causality; potential bias in anemia testing sensitivity/specificity
2	(Misunas et al., 2024)	Multi-SSA (51 countries)	Cross-sectional (DHS)	104,167	Hormonal contraceptives	Anemia (mild, moderate, severe)	Hormonal users less likely to be anemic; AOR=0.72 (0.66–0.79, p<0.001); moderate/severe anemia AOR=0.68 (0.60–0.77, p<0.001)	Cross-sectional, unable to assess causality; limited menstruation data
3	(Gedfie et al., 2022)	Ethiopia	Comparative cross-sectional	240	DMPA, implant, COC	Hematologic parameters (platelets, RBC)	Platelet count: COC 285 (IQR 238–332) vs DMPA 246 (IQR 220–226, p=0.010); implant negative correlation with RBC (p=0.033)	Cross-sectional, causality limited; single-center study
4	(Stevens et al., 2022)	Ethiopia	Observational cohort	1,200	Injectables	Discontinuation due to side effects (anemia-related)	Discontinuation rate 22% higher in anemic women (AOR=1.22, 95% CI 1.03–1.45, p=0.023)	Limited generalizability; self-reported side effects

5	(Teshome et al., 2022)	Ethiopia	DHS secondary analysis	12,981	Modern hormonal methods	Anemia (Hb <12 g/dL)	AOR=0.68 (0.62–0.75, p<0.001); implants AOR=0.72 (0.60–0.86, p<0.001)	Secondary data limitations; no longitudinal follow-up
6	(Gona et al., 2021)	Zimbabwe	DHS time-series analysis	7,634–9,235	Modern methods (not specified)	Anemia (Hb <11/12 g/dL)	Prevalence 37.8% (2005) to 27.8% (2015); HIV+ OR=2.40–2.48 (p<0.05)	Cross-sectional, no specific contraceptive effect isolated
7	(Haile et al., 2017)	Tanzania	Population-based cross-sectional	3,284	Hormonal contraceptives	Iron status (anemia)	Hormonal use associated with lower anemia risk (AOR=0.80, 0.68–0.94, p=0.007)	Cross-sectional; limited dietary data
8	(Kantarama, et al., 2025)	Rwanda	Prospective cohort	65	DMPA	Lipids (TG, HDL, TC/HDL), HbA1c, BP, hs-CRP	TG Δ +0.38 mmol/L (p=0.001); HDL Δ -0.19 mmol/L (p=0.001); TC/HDL Δ +2.45 (p=0.001); HbA1c Δ +0.3% (p=0.01)	Small sample; loss to follow-up (7/65)
9	(Turki et al., 2023)	Ethiopia	Comparative cross-sectional	186	POP, DMPA, Implanon	Lipids (TC, TG, HDL, LDL)	TC Δ +13.52 mg/dL (p<0.001); TG Δ +10.14 mg/dL (p<0.001); DMPA TC 169.51±15.82 mg/dL (p<0.001)	Cross-sectional, causality limited; single-center
10	(Kofale et al., 2023)	Ethiopia	Cross-sectional	220	COC	FBG, BP, BMI, weight	FBG Δ +2.9% (p=0.025); MAP Δ +2.5% (p=0.04); BMI Δ +3.9% (p=0.003)	Cross-sectional; small sample; self-reported data
11	(Jimoh et al., 2021)	Nigeria	Comparative study	225	COC	Lipids, BP, AIP	LDL Δ +12.4 mg/dL (p=0.038); AIP Δ +0.15 (p=0.004); SBP Δ +4.2 mmHg (p=0.02)	Short evaluation period; no long-term follow-up

12	(Shiferaw et al, 2021)	Ethiopia	Comparative cross-sectional	146	Progestin-only (DMPA, implant)	BMI, BP, lipids (TC, LDL, TG)	BMI Δ +1.2 kg/m ² (p=0.045); SBP Δ +3.8 mmHg (p=0.027); TC Δ +15.6 mg/dL (p=0.005)	Small sample; cross-sectional design
13	(Bakesiima et al., 2018)	Uganda	Cross-sectional	384	Hormonal contraceptives	Dyslipidemia	Prevalence 63.3% (95% CI 58.4–68.1); BMI PR=1.33 (1.15–1.54, p<0.001)	Non-probability sampling; no control group
14	(Kantarama et al., 2023)	Rwanda	Prospective cohort	90	DMPA	WC, lipids, HbA1c, hs-CRP, BP	TC Δ +0.52 mmol/L (p<0.05); HbA1c Δ +0.8% (p<0.05); WC Δ +2.1 cm (p=0.03)	Self-report bias; loss to follow-up
15	(Fekadi et al., 2016)	Ethiopia	Observational/Comparative	150	DMPA	Lipids	TC Δ +10.2 mg/dL (p=0.01); LDL Δ +8.7 mg/dL (p=0.02)	Small sample; no control for confounders
16	(Asare et al., 2014)	Ghana	Cross-sectional	95	OCs, injectables, implant	Lipids, CV indices	TC 4.07±0.91 vs 3.35±0.62 mmol/L (p=0.002); LDL 2.38±0.84 vs 1.74±0.57 mmol/L (p=0.003)	No dietary data; cross-sectional
17	(Ac et al, 2003)	Nigeria	Comparative study	80	Hormonal contraceptives	Lipids	TC Δ +9.8 mg/dL (p=0.04); HDL Δ -5.2 mg/dL (p=0.03)	Limited sample size; no long-term data
18	(Olumuyiwa et al., 2018)	Nigeria	Comparative cross-sectional	100	Etonogestrel (Implanon)	Lipids	HDL Δ +6.3 mg/dL (p=0.02); no significant TC, LDL changes	Small sample; short follow-up
19	(Bawah et al., 2018)	Ghana	Cross-sectional	120	Various contraceptives	Lipids, CV risk	TC Δ +11.5 mg/dL (p=0.01); LDL Δ +9.1 mg/dL (p=0.02)	Cross-sectional; no control group
20	(Sufa et al., 2019)	Ethiopia	Cross-sectional	200	Hormonal contraceptives	Dyslipidemia	Prevalence 48.2% (95% CI 41.5–55.0); OR=2.1 (1.4–3.2, p=0.001)	No dietary control; cross-sectional

21	(Adekunle et al., 2000)	Nigeria	Clinical study	60	Nomegestrol acetate (Uniplant)	Lipids (cholesterol, TG, lipoproteins)	No significant changes in TC, TG, HDL, LDL (p>0.05)	Small sample; short duration
22	(Aisien and Idogun, 2016)	Nigeria	Comparative study	90	Etonogestrel (Implanon)	Lipids, Hb	Hb Δ +0.7 g/dL (p=0.03); HDL Δ +5.8 mg/dL (p=0.04)	Small sample; no long-term follow-up
23	(Habyarimana et al., 2022)	Rwanda	Cross-sectional	88	Implant, Depo-Provera, progesterone, combined	Lipids (HDL, TG, TC, LDL)	LDL OR=11 (5.2–23.1, p=0.01); TC OR=14 (6.5–29.8, p=0.018); TG OR=2.8 (1.3–6.0, p=0.02)	Small sample; cross-sectional
24	(Marc Bertrand et al., 2024a)	Cameroon	Cross-sectional	231	Hormonal methods	Metabolic syndrome	Prevalence 58.82% (95% CI 52.3–65.2, p=0.63)	Cross-sectional; limited confounder control
25	(Avenant et al., 2024)	South Africa	Secondary analysis of RCT (WHICH)	435	DMPA-IM, NET-EN	Testosterone, SHBG	Testosterone Δ -24.3% DMPA (p<0.0001); -54.1% NET-EN (p<0.0001); SHBG Δ -29.8% DMPA, -65.1% NET-EN (p<0.0001)	Recall bias; specific population (HIV+)
26	(Singatamadliki et al., 2024)	South Africa	Randomized trial (WHICH)	521	DMPA-IM, NET-EN	Estradiol, depression, sexual behavior, menstrual effects	Estradiol Δ -60% DMPA, -62% NET-EN (p<0.001); amenorrhoea RR=1.12 (1.02–1.23, p=0.016)	Small sample for some outcomes; high loss to follow-up
27	(Hofmeier et al., 2024)	Multi-SSA	Ancillary analysis of RCT (ECHO)	398	DMPA-IM, LNG implant	Testosterone, SHBG, free testosterone	Testosterone Δ -28.35% DMPA vs IUD (p<0.001); SHBG Δ -50.04% implant vs IUD (p<0.001)	Early closure reduced power; specific population (HIV risk)
28	(Haddad et al., 2023)	Malawi	Observational with lab analyses	120	Hormonal contraceptives	Cervicovaginal cytokines, microbiota	Increased IL-6, IL-8 in hormonal users (p<0.05); altered microbiota diversity	Small sample; observational design

29	(Bunjun et al., 2022)	South Africa	Randomized trial	80	DMPA-IM	Th17-like HIV target cells	Increased Th17-like cells in DMPA users (p=0.02)	Small sample; short-term study
30	(Singata-Madliki et al., 2021)	Multi-SSA	Ancillary study of RCT	552	DMPA-IM, LNG implant	HIV acquisition, menstrual symptoms, sexual behavior	Amenorrhea higher in progestins (p<0.001); intra-menstrual coitus lower DMPA (RR=0.78, 0.68–0.89, p<0.001)	High loss to follow-up; specific population
31	(Morris et al., 2020)	Multi-SSA	RCT cohort analysis	7,829	DMPA-IM, LNG implant	Early HIV disease progression	No significant effect on HIV progression (p>0.05)	Limited power for rare outcomes
32	(Noguchi et al., 2015)	South Africa	Prospective cohort	3,147	Injectable progestins	HIV acquisition risk	DMPA HR=1.41 (1.06–1.89, p=0.02)	Observational; potential confounding
33	(Myer et al., 2007).	South Africa	Prospective cohort	4,200	Hormonal contraceptives	HIV infection risk	No significant association (HR=1.12, 0.89–1.42, p=0.33)	Limited power; self-reported use
34	(Todd et al., 2020)	South Africa	Randomized controlled trial	199	LNG-IUS	gVL, pVL, discontinuation	gVL AOR=0.78 (0.44–1.38, p=0.39); continuation 78%; expulsion C-IUD 8% vs LNG 1% (p=0.02)	Small sample; high loss to follow-up
35	(Kakaire et al., 2015a)	Uganda	Randomized controlled trial	703	LNG-IUS	Discontinuation, side effects	Discontinuation 8.6% copper vs 8.1% LNG (RR=1.1, 0.64–1.96, p=0.71)	Limited follow-up duration
36	(Harryarsad et al., 2023)	South Africa	Prospective cohort	162	Injectables, LARC	STI prevalence/incidence (CT, NG, TV, MG, HSV-2)	STI incidence 107.9/100 wy; CT 75.9/100 wy (18–21 yrs) vs 17.4/100 wy (26–33 yrs, p=0.049)	Small sample; no control group
37	(Deese et al., 2021)	Multi-SSA	Randomized cohort comparison	7,829	DMPA-IM, LNG implant	STI prevalence (chlamydia)	PR=0.90 DMPA vs IUD (0.79–1.04, p=0.16)	High loss to follow-up; specific population

38	(Kiweewa et al., 2019)	Multi-SSA	Prospective study	2,326	Injectables, implants	STI acquisition	No significant association (HR=1.15, 0.92–1.44, p=0.22)	Observational; potential confounding
39	(Kakaire et al., 2015b)	Uganda	Randomized controlled trial	703	IUD (with STI screening)	IUC removal, unscheduled visits	Removal IRR=1.1 (0.63–1.93, p=0.72); PID incidence 5 cases	Partner STI not assessed; small sample
40	(Matubu et al., 2021)	Zimbabwe	Laboratory immunology study	60	DMPA-IM, NET-EN	Cytokine production	Increased IL-1 β , IL-6 in DMPA users (p<0.05)	Small sample; in vitro study
41	(Balle et al., 2020)	South Africa	Randomized trial	130	Hormonal contraceptives	Vaginal microbiota, cytokines	Increased cytokines in CCVR (p<0.05); reduced lactobacilli	Small sample; short-term study
42	(Konstantinus et al., 2020)	South Africa	Randomized crossover study	130	NET-EN, COC, CCVR	Cervical Th17 phenotype	Lower Th17 in CCVR (p=0.001); no significant NET-EN, COC effect	Small sample; crossover design complexity
43	(Crucitti et al., 2018)	Rwanda	Randomized open-label longitudinal	120	Contraceptive vaginal ring	BV (Nugent), microbiota	Nugent score decrease (p<0.001); lactobacilli increase (p=0.031–0.041)	Small sample; open-label design
44	(Ngcapu et al., 2015)	South Africa	Observational laboratory study	85	Injectable hormonal contraception	Chemotactic cytokines	Lower IL-8, MIP-1 α in injectables (p<0.05)	Small sample; observational
45	(Avenant et al., 2023)	South Africa	RCT	435	DMPA-IM, NET-EN	Progestin levels, BMI, weight	MPA 6.59 nM; NET 13.6 nM; negative correlation with BMI (p<0.05)	Recall bias; specific population (HIV+)
46	(Kiweewa Matovu et al., 2022)	Uganda	Prospective cohort	265	DMPA (with TDF-based ART)	Bone loss	BMD Δ -2.8% in DMPA+ART vs -1.1% ART alone (p=0.01)	Small sample; specific population (HIV+)
47	(Singata-Madliki)	Multi-SSA	Ancillary study of RCT	552	DMPA-IM, LNG implant	Depression, sexual function	No significant depression increase (p>0.05);	High loss to follow-up; specific population

	et al., 2021)						sexual function unchanged	
48	(Arowojolu, et al., 2002)	Nigeria	Randomized controlled trial	150	Levonorgestrel (emergency contraception)	Bleeding disturbances, nausea	Irregular bleeding 15% (p=0.04); nausea 12% (p=0.06)	Small sample; short-term study
49	(Sagay, et al., 2002)	Nigeria	Comparative clinical study	80	Levonorgestrel (Norplant)	Electrocardiographic changes	Prolonged QT interval in 10% (p=0.03)	Small sample; no control group
50	(Isichei et al., 2000)	Nigeria	Preliminary clinical investigation	30	RICOM-1013-J (Ricinus communis)	Chemical pathological effects	No significant liver, kidney function changes (p>0.05)	Small sample; preliminary study
51	(Coutinho et al., 2000)	International (incl. SSA)	Multicenter dose-finding study	150	Gossypol (male contraceptive)	Toxicity, spermatogenesis inhibition	Hypokalemia in 5% (p=0.02); no significant liver/renal effects	Small SSA sample; male-focused