

Unintended Pregnancy and Contraception among African women living with HIV: baseline analysis of the multi-country US PEPFAR PROMOTE cohort

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Abstract

Background: About 90% of unintended pregnancies are attributed to non-use of effective contraception – tubal ligation, or reversible effective contraception (REC) including injectables, oral pills, intra-uterine device (IUD), and implant. We assessed prevalence of unintended pregnancy and factors associated with using RECs, and Long-Acting-Reversible-Contraceptives (LARCs) – implants and IUDs, among women living with HIV (WLHIV) on antiretroviral therapy (ART).

Methods: Cross-sectional analysis of US-PEPFAR PROMOTE cohort enrollment (December 2016 to June 2017) data, from Malawi, South Africa, Uganda, and Zimbabwe. Wilcoxon Rank Sum and Fisher's exact tests were used to compare continuous and categorical variables. Separate outcome (REC and LARC) modified-Poisson regression models were used to estimate prevalence risk ratio (PRR) and corresponding 95% confidence interval (CI).

Results: Of 1,987 enrolled WLHIV, 990 (49.8%) reported their last/current pregnancy was unintended; 1,027/1,254 (81.9%) non-pregnant women with child-bearing potential reported current use of effective contraception including 215/1,254 (17.1%) LARC users. Compared to Zimbabwe, REC rates were similar in South Africa, aPRR=0.97 (95% CI: 0.90-1.04), p=0.355, lower in Malawi, aPRR = 0.84 (95% CI: 0.78-0.91), p<0.001, and Uganda, 0.82 (95% CI: 0.73-0.91), p<0.001. Additionally, REC use was independently associated with marriage/stable union, aPRR=1.10 (95% CI: 1.01-1.21), p=0.039; no desire for another child, PRR = 1.10 (95% CI: 1.02-1.16), p=0.016; infrequent sex (none in the last 3 months), aPRR = 1.24 (95% CI: 1.15-1.33), p<0.001; HIV load (≤ 1000 copies/ml), PRR = 1.10 (95% CI: 1.02-1.19), p=0.014, and education (secondary or higher), aPRR = 0.91 (95% CI: 0.84-0.98), p=0.013. LARC use was independently associated with country (Zimbabwe ref: South Africa, PRR = 0.39 (95% CI: 0.26-0.57), p<0.001; Uganda, PRR = 0.65 (95% CI: 0.42-1.01), p<0.054; and Malawi, aPRR = 0.87 (95% CI: 0.64-1.19), p=0.386); HIV load (≤ 1000 copies/ml), aPRR = 1.73 (95% CI: 1.26-2.37), p<0.001; and stay home / no formal income, aPRR = 0.5 (95% CI: 0.59-0.97), p=0.027.

Conclusions: We observed high rates of unintended pregnancy and considerable gaps in use of effective contraceptives particularly LARCs. Integrated HIV and reproductive health country-level efforts to improve effective contraceptive utilization should consider HIV load, and social factors regarding education, sexual activity, sexual partnerships, fertility desires, and economic independence.

Introduction

Sub-Saharan Africa is disproportionately affected by HIV and sexual and reproductive health (S&RH) related morbidity/mortality burdens, accounting for more than 90% of the antiretroviral therapy (ART) and S&RH needs globally. [1], [2] About 60% of adults living with HIV are women of reproductive age, and reports from several countries in the region suggest that about half of pregnancies are unintended, [1]–[3] a situation potentially aggravated by the COVID-19 pandemic travel restrictions and supply disruptions. [4] The majority (90%) of unintended pregnancies in the region among women with contraceptive need are attributed to non-use of effective contraception. [5] The World Health Organization classifies contraception methods associated with less than 1% failure (unintended pregnancy) rate in the first year as very effective. These include tubal ligation, vasectomy, implants, IUD, injectables, and methods that require consistent and correct user action such as oral pills and six-month lactational amenorrhea. The second-tier methods associated with 1–9% failure rates are classified as effective and include consistent and correct use of condoms and calendar methods.[6] Both the IUD and implant classified as long-acting reversible contraceptives (LARCs) are the most effective reversible contraception for prevention of unintended pregnancy and the associated abortion risks and short pregnancy intervals.[6]–[8]

While unmet contraception need is defined as non-use of any contraception among women with a desire to avoid pregnancy,[9] about six-in-ten women in the region have an unmet need for effective contraception. Traditional methods such as periodic abstinence, withdrawal, breastfeeding or douching which remain relatively common in these settings, are unreliable and associated with high contraceptive failure rates.[10] Common reasons for effective contraception non-use include infrequent-sex, safety/side-effects/inconvenience, postpartum amenorrhea/breastfeeding, and partner or access related reasons.[11]

Among women living with HIV (WLHIV) in Africa, reproductive health decision-making and attitudes towards pregnancy-intent are potentially further complicated by unique and dynamic factors. For example, ART initiation in women with very low CD4 cell counts was associated with changes in fertility desires upon realization of improved chances of delivering an HIV-free baby, resumption of sexual libido with improving health, and social-economic and partner-related expectations.[12]–[15]

Unfortunately, a high frequency of rapid repeat pregnancies would potentially derail concerted efforts towards elimination of mother-to-child transmission of HIV, as well as undermine the overall goal of ART programs to maintain maternal and child health. Unintended pregnancies are associated with adverse obstetric outcomes such as pre-term delivery and low birth weight, and maternal complications including maternal depression and maternal depletion syndrome – a state of poor maternal and fetal/child health attributed to nutritional stress as a result of rapid repeat pregnancy with short pregnancy intervals and limited recovery times.[16]–[18] This article describes the reported intendedness of last pregnancy and factors associated with using effective contraceptives in a multi-site cohort of African WLHIV with more than 5 years on ART in four of the highest burden countries in sub-Saharan Africa.

Methods

Study Population:

This was a cross-sectional analysis of the PROMOTE (*PROMise Ongoing Treatment Evaluation*) baseline (study entry) data. The PROMOTE study was a five-year follow-up of WLHIV to assess long-term maternal health and the study design and procedures were previously described. [19] Eligible participants were enrolled between December 2016 and June 2017 at eight research sites in Malawi, Uganda, South Africa, and Zimbabwe. Study participants were sourced from the completed PROMISE (Promoting maternal and Infant Survival Everywhere) trial. [20], [21] In summary, PROMOTE study eligibility criteria included residence stability with no plans to migrate during the study follow-up period; and written informed consent for mother and/or child provided by the mother/caregiver. Both local and US affiliated Institutional Review Boards provided ethical research oversight. The study was funded by the United States Presidential Emergency Program for AIDS Relief (US-PEPFAR).

PROMOTE Study procedures

Standardized questionnaires were used to collect sociodemographic, reproductive-health, and clinical data. All women were screened for pregnancy based on self-reported last normal menstrual period dates, obstetric examination and/or laboratory detection of human chorionic gonadotropin (hCG) hormone in the urine per standard-of-care guidance and locally available commercial urine hCG test kits. Trained study staff provided ongoing ART and effective contraception counseling and linkage-to-care (outside the study) per country-specific guidelines.

Statistical Methods:

This was a planned cross-sectional analysis of the baseline PROMOTE study data. The outcome of interest was effective contraceptive use analyzed separately as reversible effective contraceptive (REC) use, and Long-Acting-Reversible-Contraceptive (LARC) use. Contraceptive type was assessed by asking current users, “*What family planning method(s) was used? (Mark all that apply)*”. Documentary evidence from the standard-of-care provider was sought to verify reported contraception method, and a certified copy was maintained on participant file. For purposes of this analysis, women who self-reported implant, IUD, injectables, or oral pills were classified as REC users; and women who reported implant or IUD methods as LARC users. Potentially effective contraceptive methods including condoms, lactational amenorrhea or calendar methods were classified as non-RECs because we did not have data to verify consistent and correct use. Other reported methods classified as non-RECs included abstinence, withdrawal, and breastfeeding.

The following characteristics which were determined *a priori* based on background knowledge and literature review were measured and analyzed to assess associations with REC and LARC use respectively. Socio-demographic factors included country of residence, age, education, household electricity use (as a measure of socio-economic status), marital/stable sexual partnerships, and employment status; reproductive-health factors included unintended last pregnancy, recent sexual activity,

future fertility desire (“*Would you like to have another child?*”), and travel time to access reproductive health services; and HIV load. Unintended last pregnancy was assessed by asking women, “*When you became pregnant this time (if currently pregnant) or last time you became pregnant, did you want to become pregnant then, or did you want to become pregnant later, or did you not want to become pregnant?*”. The last pregnancy was classified as unintended if a woman reported it was unintended, or wanted it delayed. To assess sexual activity, women were asked, “*In the last 3 months did you have sexual intercourse?*” and a “no” response was classified as infrequent sexual activity.

Overall, and country specific descriptive summary statistics were analyzed using proportions for categorical variables and median (inter-quartile range [IQR]) for continuous and discrete variables. Wilcoxon Rank Sum and Fisher’s exact test were used to compare continuous or discrete and categorical variables, respectively, across REC or LARC groups. Separate REC and LARC outcome multivariable modified Poisson regression models measured point and 95% confidence interval (CI) prevalence risk ratio (PRR) estimates, and corresponding *p*-values based on two-sided hypothesis tests with type-1 error ($\alpha = 0.05$). Based on epidemiological rationale which were specified *a priori* we included all the above-mentioned variables in the multivariable regression models. Variables were analyzed as follows: country (ref: Zimbabwe versus Malawi, Uganda, South Africa); age group (ref: ≥ 30 years versus 20–24, 25–29); unintended last pregnancy (ref: no); desire for another child (ref: yes versus no, not sure); infrequent sexual activity (no sex in last 3 months versus yes); married/ regular partner (ref: single/ divorced/ widowed/ separated); secondary education and beyond (ref: primary or no education); stay-home / no formal income (ref: formal employment/self-employed); no household electricity use (ref: yes); clinic travel time ≥ 1 hour (ref: < 1 hour); and HIV load ≤ 1000 copies/ml (ref: >1000). Data were analyzed using SAS, version 9.4(SAS Institute Inc).

Results

Study profile and population characteristics:

A total of 1,987 WLHIV were enrolled. Overall, 1,944 (97.8%) women reported currently taking ART with similarly high proportions reported across sites. The median (IQR) ART duration at PROMOTE study entry was 5 (4–5) years. The majority 1,462 (84.7%) reported currently taking efavirenz (EFV) based ART. A high ($> 90\%$) proportion of EFV-based ART was uniform across countries except for Uganda with 26.2% reporting EFV based ART, 51.0% lopinavir/ritonavir-based ART, and 22.8% were using other regimens. Overall, 70 (3.5%) women had WHO class 3 or 4 HIV clinical disease. The median CD4 cell count was high, 825.5 cells/uL, which was statistically different across countries (Uganda: 963.5 cells/uL; Malawi: 739 cells/uL; Zimbabwe: 911.5 cells/uL; South Africa: 794 cells/uL; $p < 0.001$). Viral load was not detectable in 1,628 (85%) of 1,680 women with viral load measures. Of the 301 women with detectable VL, 78 had VL less than 200 copies/ml, 21 had VL between 200–399 copies/ml, 31 had VL between 400–1000 copies/ml and 171 women had VL greater than 1000 copies/ml.

Of the enrolled women, 215 (10.8%) were currently pregnant or 6 weeks post-partum, 1,765 (88.8%) non-pregnant women had a biological potential to become pregnant, while 7 (0.4%) non-pregnant women had a prior hysterectomy or tubal ligation. (See Fig. 1). Non-pregnant women with a pregnancy potential and whose current contraception use data were available ($n = 1,254$) contributed to the contraception use analysis. Demographic, socio-economic, and reproductive health characteristics are summarized by REC use (see Table 1). The median [IQR] age was 31 [28–35] years. Most (78.2%) women had completed primary education, about half (45.0%) were either unemployed or stay-at-home. While majority (87.8%) were married or in a regular partnership, only 10% reported sexual activity in the previous 3 months, and about one-in-three desired another child. The distributions of country ($p < 0.001$), unintended last pregnancy (53.0% vs. 43.8%, $p = 0.013$), sexual activity (11.8% vs. 2.6%, $p < 0.001$), and desire for another child (34.3% vs. 48.2%, $p < 0.001$) were heterogenous across REC use categories. Age, education, employment, household electricity, marital status, clinic travel time, surviving children, ART initiation, and viral load were homogenous distributed by REC status. Similar distribution patterns were observed in the subset of women ($n = 511$ (29.0%)) who did not have reproductive-health data and were excluded from the correlates of contraceptive use analysis. Prevalence of unintended last pregnancy:

Table 1
Study population characteristics at study enrolment among women with pregnancy potential, by reversible effective contraception (REC) use

Characteristics	Overall (N = 1,254)	REC use (N = 1,027)	No REC use (N = 227)	P-value
Maternal characteristics				
Country, n (%)				< 0.001
Uganda	183 (14.6)	132 (12.9)	51 (22.5)	
Malawi	425 (33.9)	338 (32.9)	87 (38.3)	
Zimbabwe	302 (24.1)	264 (25.7)	38 (16.7)	
South Africa	344 (27.4)	293 (28.5)	51 (22.5)	
Age (years), median [IQR]	31 (28–35)	31 (28–35)	30 (26–35)	0.095
Age group (years), n(%)				0.114
20–24	122 (9.7)	93 (9.1)	29 (12.8)	
25–29	360 (28.7)	290 (28.2)	70 (30.8)	
≥ 30	772 (61.6)	644 (62.7)	128 (56.4)	
Highest level of education, n(%)				0.477
None/Primary	273 (21.8)	228 (22.2)	45 (19.8)	
Secondary and higher	981(78.2)	799 (77.8)	182 (80.2)	
Employment, n (%)				0.995
Formal employment	292 (23.3)	239 (23.3)	53 (23.3)	
Self-employment (small business)	396 (31.6)	325 (31.7)	71 (31.3)	
Not formally employed/housewife	564 (45.0)	461 (45.0)	103 (45.4)	
Electricity in household, n (%)	872 (69.5)	707 (68.8)	165 (72.7)	0.266
Married/regular partner, n (%)	1101 (87.8)	904 (88.0)	197 (86.8)	0.577
Unintended last pregnancy, n (%)	643 (51.4)	544 (53.0)	99 (43.8)	0.013
No sex in the last 3 months, n (%)	127 (10.1)	121 (11.8)	6 (2.6)	< 0.001
Desire for another child, n (%)				< 0.001
Yes	461 (36.8)	352 (34.3)	109 (48.2)	
No	711 (56.7)	606 (59.0)	105 (46.5)	
Not sure	81 (6.5)	69 (6.7)	12 (5.3)	
Clinic travel time < 1 hour, n (%)	902 (72.0)	751 (73.1)	151 (66.8)	0.06
Number of surviving children, median (IQR)	3 (2–3)	3 (2–3)	2 (2–4)	0.100

Key: REC – Reversible Effective Contraceptives including oral, injectable, intra-uterine device (IUD), or implants; [5] IQR, Interquartile range; ^a p-value from Wilcoxon rank-sum test; ^b p-value from Fisher's exact test. Highlighted p-values are statistically significant. The number of participants with missing data was minimal: pregnancy-intent (n = 2); employment (n = 2); maternal-age (n = 1); fertility desire (n = 1); clinic travel-time (n = 1); surviving children (n = 2); CD4 count (n = 9) and no missing data on education; electricity-use; marital-status; sexual history; ART status; and viral load.

Characteristics	Overall (N = 1,254)	REC use (N = 1,027)	No REC use (N = 227)	P-value
Number of surviving children, n(%)				0.211
0–2	594 (47.4)	478 (46.6)	116 (51.3)	
658 (52.6)	548 (53.4)	110 (48.7)		
Currently on ART, n (%)	1223 (97.5)	1002 (97.6)	221 (97.4)	0.814
Viral load ≤ 1000 copies/ml, n (%)	1142 (91.1)	929 (90.5)	213 (94.2)	0.071
CD4 count (cells/mm ³), median (IQR)	826 (648–1039)	829 (649–1041)	814.5 (643–1027)	0.859
Key: REC – Reversible Effective Contraceptives including oral, injectable, intra-uterine device (IUD), or implants; [5] IQR, Interquartile range; ^a p-value from Wilcoxon rank-sum test; ^b p-value from Fisher’s exact test. Highlighted p-values are statistically significant. The number of participants with missing data was minimal: pregnancy-intent (n = 2); employment (n = 2); maternal-age (n = 1); fertility desire (n = 1); clinic travel-time (n = 1); surviving children (n = 2); CD4 count (n = 9) and no missing data on education; electricity-use; marital-status; sexual history; ART status; and viral load.				

At enrollment, 177/1,987 (8.9%) women were pregnant, of these 80 (45.2%) reported it was unintended. Overall, 990/1987 (49.8%) of the enrolled women reported their last pregnancy was unintended. Of these, 409 (41.3%) reported pregnancy was mistimed and 581 (58.7%) pregnancy was unwanted. There were site differences ($p < 0.001$). The highest prevalence of unintended last pregnancy was observed at the South African sites (Durban [81.9%], and Soweto [55.7%]); followed by the Malawi sites (Lilongwe [57.5%], and Blantyre [51.3%]); the Zimbabwe sites ranged from 29.8–41.9%; and 28.4% at the Uganda site.

Reported contraceptive use:

Among 1,254 (63.1%) WLHIV who were not pregnant at enrolment and with a biological potential to become pregnant and with available contraceptive data), 1,027 (81.9%) self-reported REC use including 215 (17.1%) on LARCs. Injectables were the commonest 43.0%, followed by condoms only 17.5%, implant 15.4%, oral pills 14.6%, tubal ligation 7.1%, and IUD 1.8%. Of the 1,027 women, 583 (56.8%) reported dual use of condoms together with another REC. There were country variations ($p < 0.001$) in REC use. Injectables were the commonest choice reported in Uganda (41.5%), Malawi (44.9%), and South Africa (60.2%), while oral pills the most reported in Zimbabwe (44.0%). A similar frequency pattern of injectables followed by condoms only, implant and oral pills, was reported in Malawi, Uganda, and South Africa. In Zimbabwe oral pills were the commonest followed by injectables, implants, and condoms only (see Fig. 2). Overall, traditional methods including abstinence, withdrawal, or breastfeeding, were the only contraception reported by about one-in-five women: highest in Uganda, 31.1% and Malawi, 24%, followed by South Africa, 17.4%, and 12.2% in Zimbabwe.

Factors associated with contraceptive (REC and LARC) use:

Separate (REC and LARC outcomes) multivariable model results are presented in Table 2. Compared to Zimbabwe, rates of REC use were similar in South Africa, aPRR = 0.97 (95% CI: 0.90–1.04), $p = 0.355$, and significantly lower in Malawi, aPRR = 0.84 (95% CI: 0.78–0.91), $p < 0.001$) and Uganda, 0.82 (95% CI: 0.73–0.91), $p < 0.001$. In addition, REC use was associated with marriage/stable union, aPRR = 1.10 (95% CI: 1.01–1.21), $p = 0.039$; no desire for another child, aPRR = 1.10 (95% CI: 1.02–1.16), $p = 0.016$; infrequent sex (no sex in the last 3 months), aPRR = 1.24 (95% CI: 1.15–1.33), $p < 0.001$; as well as controlled HIV load below or equal to 1000 viral copies/ml, aPRR = 1.10 (95% CI: 1.02–1.19), $p = 0.014$. However, women with secondary and higher education were less likely to report REC use, aPRR = 0.91 (95% CI: 0.84–0.98), $p = 0.013$.

Table 2
Factors associated with use of contraceptive methods (REC/ LARC) reported at PROMOTE study entry

	REC use		LARC use	
	Adjusted PRR (95% CI)	P value	Adjusted PRR (95% CI)	P value
Country (ref: Zimbabwe)				
Malawi	0.84 (0.78–0.91)	< 0.001	0.87 (0.64–1.19)	0.386
South Africa	0.97 (0.90–1.04)	0.355	0.39 (0.26–0.57)	< 0.001
Uganda	0.82 (0.73–0.91)	< 0.001	0.65 (0.42–1.01)	0.054
Age group (years) (ref: ≥30)				
20–24	0.95 (0.85–1.05)	0.307	0.87 (0.54–1.39)	0.552
25–29	1.00 (0.94–1.06)	0.950	1.19 (0.91–1.56)	0.211
Unintended last pregnancy (ref: no)	0.97 (0.91–1.02)	0.192	0.89 (0.70–1.14)	0.366
Desire another child (ref: Yes)				
No	1.10 (1.02–1.16)	0.016	0.93 (0.71–1.23)	0.680
Unsure	1.10 (0.98–1.21)	0.097	0.84 (0.48–1.45)	0.527
Infrequent sex (self-reported no sex in last 3 months)	1.24 (1.15–1.33)	< 0.001	1.03 (0.69–1.53)	0.861
Married/ regular partner (ref: single/ divorced/widowed/separated)	1.10 (1.01–1.21)	0.039	0.79 (0.56–1.10)	0.159
Secondary and beyond (ref: primary or no education)	0.91 (0.85–0.98)	0.013	0.82 (0.60–1.11)	0.199
Stay home women/ no formal income (ref: formal/self-employment)	0.96 (0.91–1.02)	0.169	0.75 (0.59–0.97)	0.027
No electricity in household	1.04 (0.98–1.11)	0.210	0.78 (0.58–1.04)	0.090
Clinic travel time ≥ 1 hour (ref: < 1 hour)	0.98 (0.91–1.04)	0.475	0.91 (0.69–1.21)	0.525
HIV load, ≤ 1000 copies/ml (ref: >1000 copies/ml)	1.10 (1.02–1.19)	0.014	1.73 (1.26–2.37)	< 0.001
<p>Key: REC – Reversible Effective Contraception including oral, injectable, intra-uterine device (IUD), or implants[5]; LARC - Long Acting Reversible Contraceptives including implant and IUD which are considered to be the most effective reversible contraception for prevention of unintended pregnancy and the associated abortion risks and short intervals between pregnancies[7], [8]; The respective multivariate regression models included all the variables listed: country (ref: Zimbabwe versus Malawi, Uganda, South Africa); age group (ref: ≥30 years versus 20–24, 25–29); unintended last pregnancy (ref: no); desire for another child (ref: yes versus no, not sure); infrequent sexual activity (no sex in last 3 months versus yes); married/ regular partner (ref: single/ divorced/ widowed/ separated); secondary education and beyond (ref: primary or no education); stay-home / no formal income (ref: formal employment/self-employed); no household electricity use (ref: yes); clinic travel time ≥ 1 hour (ref: < 1 hour); and HIV load ≤ 1000 copies/ml (ref: >1000).</p>				

Regarding use of LARCs, lower rates were observed in South Africa, Malawi, and Uganda relative to Zimbabwe; significantly lower in South Africa, aPRR = 0.39 (95% CI: 0.26–0.57), $p < 0.001$, borderline significance in Uganda, aPRR = 0.65 (95% CI: 0.42–1.01), $p < 0.054$, while the lower rates in Malawi were not statistically significant, aPRR = 0.87 (95% CI: 0.64–1.19), $p = 0.386$. Additionally, LARC use was associated with HIV load (below or equal to 1000 viral copies/ml), aPRR = 1.73 (95% CI: 1.26–2.37), $p < 0.001$; while stay home women or those reporting no formal income were less likely to report LARC use, aPRR = 0.75 (95% CI: 0.59–0.97), $p = 0.027$.

Discussion

These cross-sectional data from a large multi-country cohort of African WLHIV on life-time ART reveal a high prevalence (about half) of unintended last pregnancy and low rates of current use of effective contraception among those with contraception need. About one-in-five women with contraceptive need reported use of traditional methods which are known to be ineffective, and use of long-acting reversible contraceptives (LARCs) was very low (~20%). Based on multivariable regression analyses, marriage/stable relationship, sexual activity, future fertility desires, relative HIV control (≤ 1000 HIV copies/ml), and education were independently associated with use of reversible effective contraceptives (RECs); but no associations were observed with age, socio-economic factors (employment, household electricity), unintended last pregnancy, and clinic travel-time. LARC use was associated with relative economic independence (formal/self-employment) and HIV-control, but not the other factors. Compared to Zimbabwe, rates of REC use were similar in South Africa but lower in Malawi and Uganda; and LARC rates were lower in South Africa, Malawi, and Uganda.

The unacceptably high unintended pregnancy rates observed in this study, which varied considerably across countries, are comparable to high prevalence (35–70%) reports from previous African WLHIV studies in similar resource-limited settings in Rwanda (2007), Botswana (2010–2012), South Africa (2009–2010), Eswatini (2010), Zimbabwe (2012), and Kenya (2016). [22]–[29] However, the extremely high prevalence observed in this study at the Umlazi, Durban site in South Africa (81.9%) has not been reported previously. Moreover, it is likely that the prevalence observed in this urban/peri-urban study population is a conservative estimate of the respective country-level burdens since access to reproductive health services in many African countries is reportedly more than two-fold higher in urban versus rural settings where the majority of the population resides. [30] It has also been reported that WLHIV in these African settings who have not initiated lifelong ART or women who are not aware of their HIV infection status have a higher likelihood of reporting unintended pregnancy. [23], [24], [29] All the women in this study were aware of their HIV infection status and the majority (>97%) had initiated life-long ART by the time they conceived the reported unintended last pregnancy. Data on contraceptive use prior to the reported unintended pregnancy was not available for this analysis which precluded assessment of other risk factors of unintended pregnancy among WLHIV reported in these settings including unmet need for effective contraceptives or contraceptive failures. [25], [26], [29]

Regarding contraceptive use in this study population, traditional methods (breastfeeding, withdrawal, abstinence, calendar, or condoms only) which are potentially ineffective particularly when used incorrectly and/or inconsistently [6], were common (~20%), and LARC use was unacceptably low. These findings are concerning particularly because this cohort of WLHIV had recently transitioned from the PROMISE trial, a controlled five year follow-up study setting during which they had the benefit of routine counselling and referral/access to standard-of-care reproductive-health clinics. [20], [21] Contemporaneous studies in these African settings reported comparable high rates of using potentially ineffective contraceptive methods and similarly low LARC use. [25], [28], [31]–[34] The high prevalence of a single contraceptive method at the respective sites is consistent with reports from other African settings, compared to other regions which tend to report relatively more diverse contraceptive method-mix. [25] [33], [35] Since our study women received their contraceptives from standard-of-care/non-study providers, the observed skewed patterns may be an artifact of the policy, provider-factors (training, bias and attitudes) or available stocks at country, regional or facility level. Unfortunately, the predominantly reported methods in this study, both injectable- and oral-contraceptive methods are heavily user-action dependent, including 3-monthly provider-clinic visits for repeat injections, or require diligently swallowing daily oral contraceptives coupled with routine provider-clinic visits for refills. Intermittent non-adherence over a protracted period of self-perceived contraceptive use may affect contraceptive effectiveness to low levels potentially comparable to non-contraceptive use.[36] Implants and IUDs, which are the most effective reversible contraceptive methods for an extended period without requiring user-action were rarely reported: only about one-in-ten of our study women reported implant use in South

Africa and Uganda, and about one-in-five in Malawi and Zimbabwe; and less than 4% reported IUDs. In these settings where provision of safe sterilization services is challenging coupled with restrictive age eligibility criteria, LARCs are important alternatives for women of any age who particularly do not want to have more children. Unfortunately, implants and IUDs require more provider skill and training. It has been suggested that women in these settings who are using short-acting hormonal methods might prefer a LARC if they had the opportunity, [37] however, busy clinics may shun provision of LARCs since they are provider-labor-intensive. For example, the low enthusiasm towards implants by providers in South Africa is attributed to a policy change that was deemed rushed with inadequate provider-training during the roll-out in 2014, followed shortly after by a policy against implant provision to women on efavirenz-based ART.[38]

Collectively, our findings of high prevalence of unintended last pregnancy coupled with subsequent low REC usage rates, particularly LARCs, underscores the need to better understand individual-level, as well as community- and facility-level factors that may influence utilization of effective contraception by WLHIV in these settings. Concerningly, unintended last pregnancy did not appear to incentivize subsequent use of RECs, an indicator of perennial contextual factors that preclude utilization. Understandably, and consistent with previous reports, factors that were independently associated with REC use included future fertility desires; [26], [32] correlates of self-perceived risk of pregnancy including sexual activity and stable/sustained sexual partnerships; [32], [39] as well as relative HIV control, [26] a proxy for good health. However, the negative association between REC use and higher education in this study is counterintuitive, similar to previous African studies linking higher education with unmet contraceptive need, [40]–[42] and another suggesting education had no influence on effective contraceptive choice. [43] A plausible explanation is that WLHIV in our study with higher education delayed childbearing since higher education was correlated with desire for another child. The considerable variations in the contraception options reported, including REC as well as LARC use, across different countries in our study, is characteristic in the region. This heterogeneity reflects the existing substantial contextual dissimilarities,[44] including level of political will and governments' investment and commitment to contraceptive services across African countries. [45] It is not surprising that age was not associated with REC or LARC use in this study considering the relatively homogenous age group with a median (IQR) 31 (28–35) years of age. This is consistent with previous studies with similar age band comparisons.[26], [40], [46] Studies that reported associations between age and contraceptive use included younger women and adolescents, a group associated with higher unmet contraception needs [32], [40]–[42]. However, these studies did not specify use of effective contraception, and while they were conducted in high HIV-burden settings, individual HIV status was not ascertained. An Ethiopian study of WLHIV reported lower use of modern contraceptives among older women above 35 years compared to their 15–24 year old counterparts. [46]

This study had some limitations. A recall bias inherent to cross-sectional surveys was likely in these analyses based on individuals thinking back and reporting their pregnancy intent, although the magnitude was likely minimal since as has been argued, pregnancy related events are relatively easier to recall given their significance in a woman's lifetime.[47] A woman's desire for a given pregnancy is fluid and intervening factors before, during and after pregnancy such as partner and/or other social-economic support, access to care, loss of the pregnancy or demise of an older child, etc., will likely influence the woman's attitude towards the pregnancy.[48]–[51] A tendency towards "retrospective rationalization" of previously undesired pregnancies has been proposed [49], [52] suggestive of underreporting of unintended pregnancy rates; although the reverse has been reported where women changed from intended to unintended pregnancy reports, in a repeated measure analysis.[53] Also, the lack of data on contraceptive-choices immediately preceding the reported unintended pregnancies precluded the ascertainment of whether the reported unintended pregnancies resulted from non-use of effective contraceptives or contraceptive failure including user-related (inconsistent or incorrect use) or method-related failures. Also, contraceptive data was not available for about 30.4% of the women enrolled before the relevant reproductive health questions were added to the baseline questionnaire. The exclusion of these women from these analyses may have potentially resulted in a selection bias. Reassuringly, the distribution of baseline characteristics was similar among the excluded women compared to those who contributed to these analyses. Nonetheless, these study findings contribute to the growing body of empirical data suggestive of reproductive health challenges that persist in resource-limited African settings, which also have a heavy HIV burden. This analysis was based on a large sample of WLHIV on life-long ART from very high burden countries. Data was well characterized including laboratory confirmation of HIV status, a challenge in previous studies which used simpler self-report data. [25]

Conclusion

Unacceptably high rates of unintended pregnancy persist among WLHIV on life-long ART; concerningly, effective contraceptive methods were not universally used among women with contraceptive need. Use of LARCS remained very low. There were considerable variations across the four eastern and southern African countries, an indication of cultural, social, and political contextual differences. Unfortunately, the persistence of reproductive health challenges does not match recent considerable improvements in access and utilization of HIV care services in the respective countries. Country level efforts should employ integrated HIV care and reproductive health services delivery, [54] while carefully considering the risk categorization: future fertility desires, sexual activity, self-perceived risk of unintended pregnancy, and socio-economic and cultural perspectives. It is imperative that WLHIV clients attending HIV care programs, including all care during pregnancy through delivery, are availed the whole spectrum of effective contraception options that are safe, user-friendly, and discrete. This is essential to uphold reproductive health rights, and to mitigate health burden due to unintended pregnancy, unsafe abortion, and lost economic productivity of women which ultimately impacts family health. [55]–[57] LARCs, including immediate provision of LARCs to postpartum mothers, [58] is a strategy that minimizes contraceptive adherence challenges attributed to user-action dependency. Research efforts to better understand potential dual protective benefits of multipurpose technologies – involving adding ART and a contraceptive agent such as levonorgestrel using barrier devices such as intravaginal rings, should be prioritized. [59]

Declarations

Ethics approval and consent to participate: The protocol was approved by the local IRBs in the participating countries in Malawi (Lilongwe and Blantyre); South Africa (Johannesburg and Durban); Uganda (Kampala) and Zimbabwe (Harare and Chitungwiza) and the collaborating institutions (Johns Hopkins University (JHU), University of North Carolina (UNC), and University of California San Francisco (UCSF)) in the USA. Prior to study enrolment, written informed consent for study participation was obtained from all eligible research volunteers.

Consent for publication: As part of the enrolment criteria, all study participants provided written informed consent for study participation, and for data dissemination of study findings including through presentation at conferences and publications.

Availability of data and materials: The data supporting these findings, and the statistical analyses scripts will be made available upon request.

Competing interests: The authors declare that they have no competing interests including financial, consultant, institutional or other relationships that might lead to a bias or conflict of interest. This work was presented in part at the 10th International Workshop on HIV Pediatrics (abstract #83), 20-21 July 2018, Amsterdam, The Netherlands.

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Authors' contributions: JA, contributed to the overall coordination of this study, took the lead in the data analysis plan and manuscript writing; NYZ conducted the overall study data management and statistical analysis for this manuscript; SH; TN; MMN; SD; LC; CN supported the coordination of study activities at their respective sites and contributed to the writing of this manuscript; MGF and TT, (Protocol Chairs), conceived of the study, contributed to the overall study design and implementation, analysis for this manuscript, and writing this manuscript. All authors read and approved the final manuscript.

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Figures

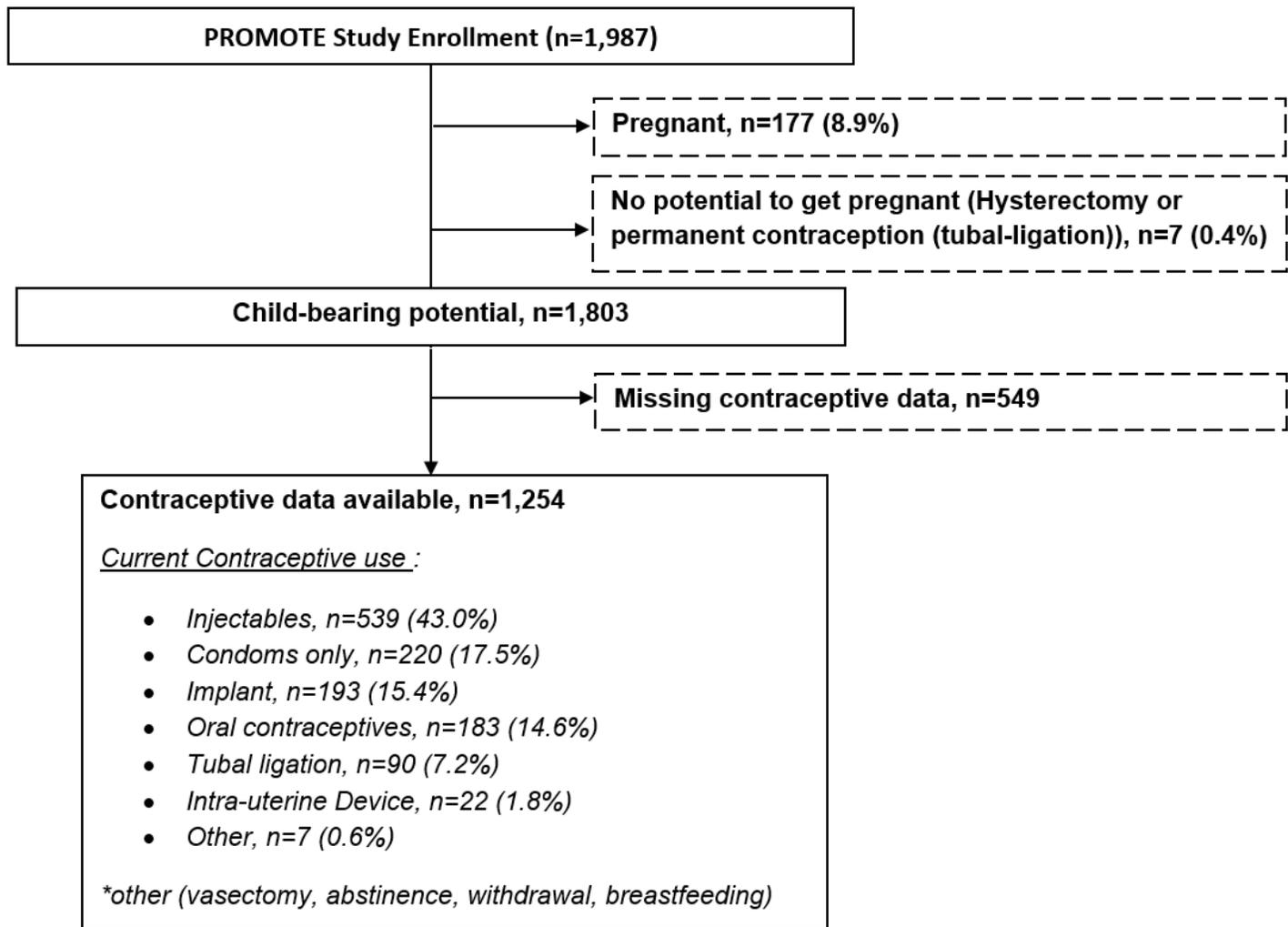


Figure 1

PROMOTE enrollments and contraceptive use reported by women with available data at baseline Key: PROMOTE - Promoting Maternal and Infant Survival Everywhere; Child-bearing potential refers to women who had no biological preclusion to becoming pregnant; Of the 1,254 women with available contraception data at baseline, every woman reported currently using at least one method to prevent getting pregnant. Contraceptive data was not available for 549 (30.4%) women who were enrolled before the relevant reproductive health questions were added to the baseline questionnaire.

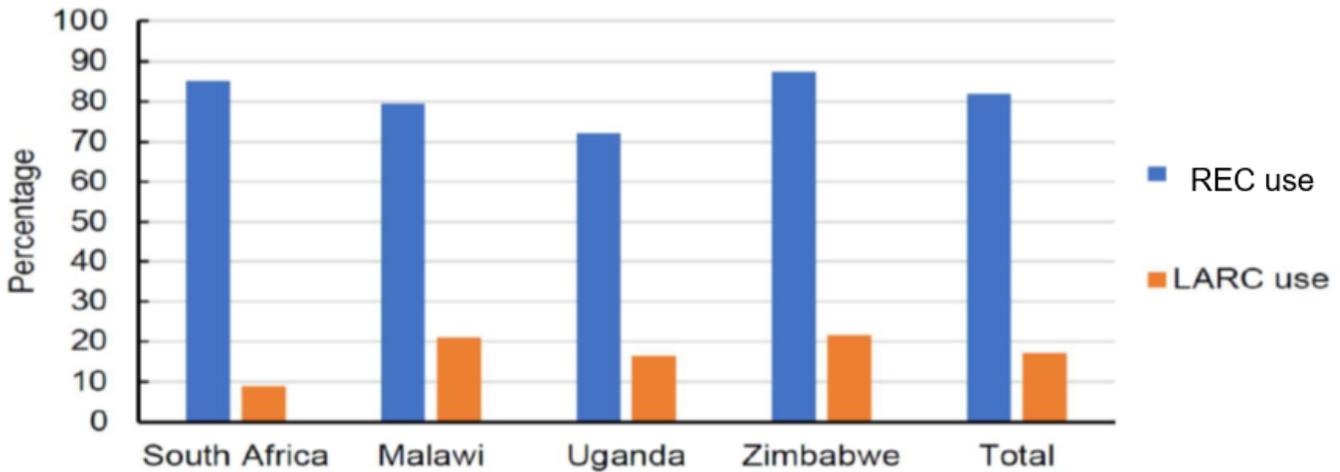
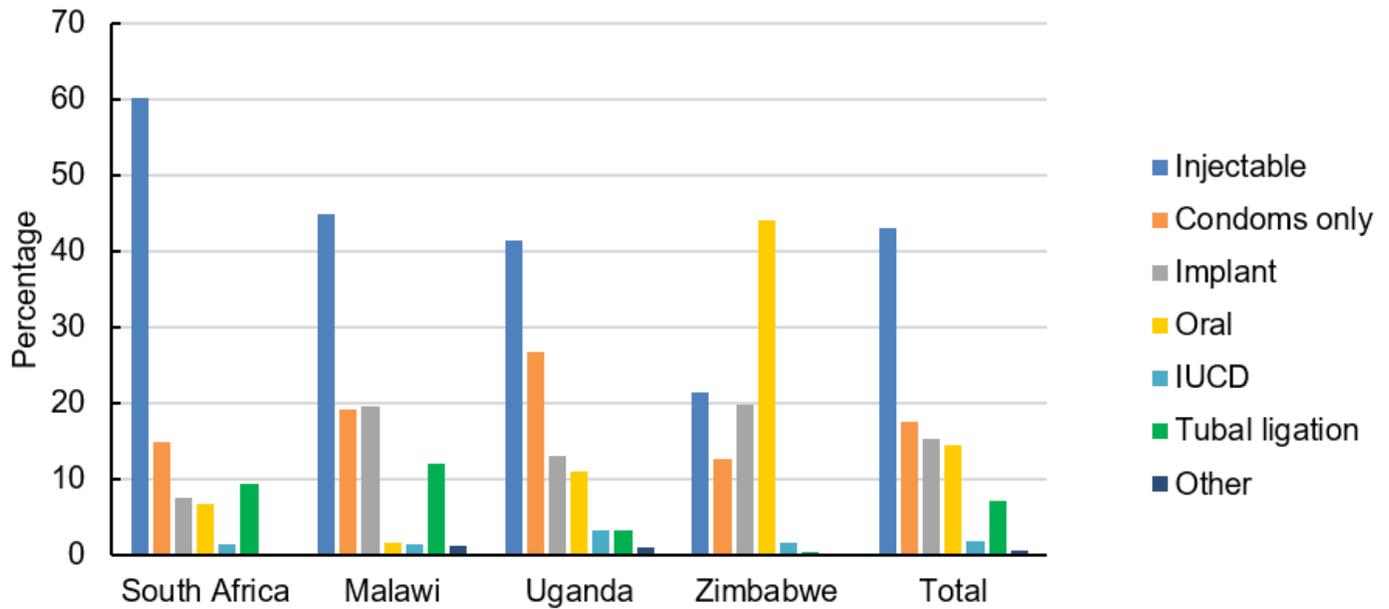


Figure 2

Contraceptive methods reported by women using contraception and with available data at PROMOTE study entry.

Key: Current contraceptive used reported by 1,254 women with available data at PROMOTE study entry. All these women reported currently using at least one method to prevent getting pregnant. REC – Reversible Effective Contraception including oral, injectable, intra-uterine device (IUD), or implants[5]; LARC - Long Acting Reversible Contraceptives including implant and IUD which are considered to be the most effective reversible contraception for prevention of unintended pregnancy and the associated abortion risks and short intervals between pregnancies[7], [8]; *The category ‘Other contraceptive methods’ includes *abstinence, withdrawal, breastfeeding*.