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# BMJ Open

## Dyslipidemias in women using hormonal contraceptives: a cross sectional study in Mulago Hospital Family Planning Clinic, Kampala

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Complete List of Authors:	Bakesiima, Ritah; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Byakika-Kibwika, Pauline; Makerere University College of Health Sciences, Department of Internal Medicine Tumwine, James; Makerere University College of Health Sciences, Department of Pediatrics and Child Health Kalyango, Joan; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Nabaasa, Gloria; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Najjingo, Irene; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Nabaggala, Grace; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Olweny, Francis; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Karamagi, Charles; Makerere University College of Health Sciences, Department of Pediatrics and Child Health
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3 **Dyslipidemias in women using hormonal contraceptives: a cross sectional**  
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5 **study in Mulago Hospital Family Planning Clinic, Kampala**  
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10 Ritah Bakesiima<sup>1</sup>, Pauline Byakika-Kibwika<sup>2</sup>, James Tumwine<sup>3</sup>, Joan N Kalyango<sup>1</sup>, Gloria  
11  
12 Nabaasa<sup>1</sup>, Irene Najjingo<sup>1</sup>, Grace S Nabaggala<sup>1</sup>, Francis Olweny<sup>1</sup>, Charles Karamagi<sup>3</sup>  
13  
14

15  
16 <sup>1</sup>Clinical Epidemiology Unit, School of Medicine, College of Health Sciences, Makerere  
17  
18 University, Kampala, Uganda  
19

20  
21 <sup>2</sup>Department of Internal Medicine, School of Medicine, College of Health Sciences, Makerere  
22  
23 University, Kampala, Uganda  
24

25  
26 <sup>3</sup>Department of Paediatrics, School of Medicine, College of Health Sciences, Makerere  
27  
28 University, Kampala, Uganda  
29

30  
31 Corresponding author: Ritah Bakesiima  
32

33  
34 (E-mail: [esmie.ritah@gmail.com](mailto:esmie.ritah@gmail.com))  
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37 +256772029182, +256706807057  
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## ABSTRACT

**Objective:** The aim of this study was to determine the prevalence and factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala.

**Design:** Cross sectional study

**Setting:** Mulago Hospital, Kampala

**Participants:** 384 women aged 18 to 49 years who had used hormonal contraceptives for at least three months and consented to participate in the study were included in the study.

**Study outcome:** Dyslipidemias defined as derangements in lipid profile levels for which the prevalence and associated factors were obtained.

**Results:** The prevalence of dyslipidemias was 63.3% (95% CI: 58.4 – 68.1), with the commonest form of dyslipidemias being elevated LDL levels ( $\geq 160$  mg/dl) in 187 (48.7%) of the participants. Body Mass Index (BMI) (PR=1.33, 95% CI: 1.15-1.54,  $p < 0.001$ ) and use of anti-retroviral therapy (ART) (PR=1.21, 95% CI: 1.03-1.42,  $p = 0.020$ ) were the factors found to be significantly associated with dyslipidemias.

**Conclusion:** Dyslipidemias were present in more than half of the participants and this increases their risk for cardiovascular diseases. The high risk groups were women with a BMI greater than 25 and women who were on ART. Lipid profiles should therefore be assessed in women using hormonal contraceptives for their better management.

**Keywords:** Hormonal Contraceptives, Contraception, Dyslipidemias, Lipid profile

### Strengths and limitations of the study

- i) This being one of the first studies in Uganda to assess dyslipidemias in women using hormonal contraceptives, the cross sectional study design used was the most appropriate to provide baseline information.

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3 ii) Standard approaches were used to carry out the study to ensure repeatability and  
4 reproducibility.  
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7 iii) Selection procedure used is non-probability so results may not be generalisable to  
8 all hormonal contraceptive users.  
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11 iv) This being a cross-sectional study, a causal relationship between hormonal  
12 contraceptive use and dyslipidemias cannot be ascertained.  
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15 v) The results may have been subject to information bias because questionnaires  
16 were used to obtain information on some variables which are based on recall.  
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## 22 INTRODUCTION

23  
24 Globally, the use of contraception has risen slightly, from 54.7% in 1990 to 64% in 2015 [1]  
25 and in Uganda particularly, the Contraceptive Prevalence Rate (CPR) is currently at 27.2%  
26 with hormonal contraceptives (HCs) accounting for 77.9% of the total contraceptive use.[1]  
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Several researchers have reported the complications and side-effects associated with the use of these hormonal contraceptives which include nausea and vomiting, headaches, dizziness, breast tenderness and enlargement, irregular bleeding or bleeding between periods, and weight gain as the side effects and adverse effects like metabolism impairment, heart and circulation complications, venous thromboembolism, an increased risk of cancer, and liver problems.[3] It has been suggested that some of the aforementioned complications are a consequence of dyslipidemias, a potential metabolic impairment effect of long term use of some of these hormonal contraceptives.[4] Furthermore, a study by Schueller and his colleagues suggested that these dyslipidemias could also rise as a result of these hormones

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3 increasing apolipoprotein B-100 synthesis which subsequently increases triglyceride and  
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5 LDL levels.[5]

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7 Several factors have been reported to predispose hormonal contraceptive users to  
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9 dyslipidemias like age, race, body weight, lifestyle, use of other medications like ART,  
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11 steroids and pre-existing diseases like hypertension, diabetes mellitus and obesity. Many of  
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13 these factors are common in Uganda. For example, 16% of the females in Uganda were found  
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15 to be obese.[6] Obesity is associated with alterations in lipid profile levels, and this, in the  
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17 presence of hormonal contraceptive use increases the risk of dyslipidemias.[7, 8] In addition,  
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19 38,484 women in Uganda were reported to be on anti-retroviral therapy (ART) between June  
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21 2010 and March 2017.[9] Some of these antiretroviral drugs alter lipid profile levels hence  
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23 bringing about dyslipidemias.[10, 11]

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26 Poorly managed dyslipidemias can result into cardiovascular diseases like venous  
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28 thromboembolism, myocardial infarction and stroke.[12] However, lipid profile levels are not  
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30 measured in women using hormonal contraceptives in Uganda because little is known about  
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32 the dyslipidemic effect of hormonal contraceptives. This study therefore aimed at  
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34 determining the prevalence and factors associated with dyslipidemias in women using  
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36 hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala.  
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## 39 40 41 **METHODS**

### 42 43 **Study design, setting and population**

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45 This was a quantitative cross sectional study employing both descriptive and analytical  
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47 techniques carried out from Mulago Hospital Family Planning Clinic, Kampala in March and  
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49 April, 2017. Using the consecutive sampling procedure, a total of 384 women aged 18 to 49  
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51 years who had used hormonal contraceptives for atleast three months and consented to  
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53 participate in the study were included in the study, and all women who were unable to  
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55 comprehend either English or Luganda and could not adhere to study procedures were  
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3 excluded from the study. For ethical considerations, necessary permission to carry out this  
4 study was obtained from all relevant bodies, informed consent obtained from all the  
5 participants before enrolment into the study and confidentiality highly maintained.  
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### 8 9 **Data collection**

10 A questionnaire was administered to collect basic information on age, parity, highest level of  
11 education, occupation, type of hormonal contraceptive used, duration of use of hormonal  
12 contraceptives, use of anti-retroviral drugs and history of hypertension. Body Mass Index  
13 (BMI) was determined by measuring weight using the Seca weighing scale and height using a  
14 stadiometer. BMI was then computed as Weight (in Kg)/Height (in metres squared). Blood  
15 samples were collected from participants after a 6 hour fast for the determination of fasting  
16 blood sugar and lipid profile levels. Lipid profile levels were assessed using the Cobas 6000  
17 Chemistry analyser.  
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### 28 29 **Outcome variable**

30 The outcome variable for this study was dyslipidemias defined as derangements in the lipid  
31 profile levels which included a total cholesterol level of 200 mg/dL or greater, a high-density  
32 lipoprotein cholesterol level of less than 40 mg/dL, a triglyceride level of greater than 150  
33 mg/dL, or a low-density lipoprotein cholesterol level of 160 mg/dL or greater according to  
34 the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III)  
35 guidelines.[13] A participant was said to have dyslipidemias if they had any of the lipid  
36 profile parameters in ranges stated above. The presence of dyslipidemias was coded as “1”  
37 and its absence as “0”.  
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### 48 49 **Statistical analysis**

50 Data were analysed using STATA version 13.0 in which all continuous variables were  
51 summarised as medians and ranges while the categorical variables were summarised as  
52 percentages and proportions. The prevalence of dyslipidemias was calculated as the  
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percentage of women with dyslipidemias over the total number of women in the study. The modified Poisson regression model was used to analyse the factors associated with dyslipidemias in women using hormonal contraceptives. In the multivariate analysis, confounders were retained only if they changed the estimates by greater than or equal to 10%. Confidence intervals were presented at 95% level of significance along with the p-values. Statistical significance was considered at a p-value of less than or equal to 0.05.

## RESULTS

### Participants' characteristics

The median age of the 384 participants was 28 years (IQR: 18 – 49) and 59.1% (227/384) of the participants had attained only up to secondary education, 74.2% (285/384) had at least two or more children and 39.6% (152/384) were self-employed. Only 11 (2.9%) had high fasting blood sugar levels ( $\geq 120$  mg/dl), 14 (3.7%) had a history of hypertension, 140 (36.5%) had a BMI  $>25$  and 78 (20.3%) were on anti-retroviral therapy (ART). Most of the participants were using Progestin-Only Injectables - 185 (48.2%) and 219 (57.0%) had used hormonal contraceptives for over a year (Table 1).

**Table 1:** Social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Number (N=384)	Percentage (%)
<b>Age</b> (Categorised at the median)		
18 – 28	215	56.0
29 – 49	169	44.0
Median (IQR): 28 (18 – 49)		
<b>Education</b>		
No formal education	14	3.6
Primary	107	27.9
Secondary	227	59.1
Tertiary	36	9.4
<b>Parity</b>		
0 - 1	99	25.8
Two or more	285	74.2

<b>Fasting Blood Sugar</b>		
Normal (<120 mg/dl)	373	97.1
High ( $\geq$ 120 mg/dl)	11	2.9
<b>History of Hypertension</b>		
No	370	96.3
Yes	14	3.7
<b>Body Mass Index (BMI)</b>		
$\leq$ 25	244	63.5
>25	140	36.5
<b>ART Use</b>		
No	306	79.7
Yes	78	20.3
<b>Hormonal Contraceptive Used</b>		
Progestin Only Pill (POP)	5	1.3
Combined Oral Pill (COP)	38	9.9
Progestin Only Injectable (POI)	185	48.2
Combined Injectable Contraceptive (CIC)	8	2.1
Implant (1 rod)	124	32.3
Implant (2 rods)	24	6.2
<b>Duration of use of HC</b>		
<6 months	124	32.3
6 to 11 months	41	10.7
12 or more months	219	57.0

### Prevalence of dyslipidemias

The prevalence of dyslipidemias amongst the 384 participants was 63.3% (95% CI: 58.4 – 68.1). Dyslipidemias were higher in women aged above 28 years – 68.0% (115/169) compared to those who were younger. The prevalence of dyslipidemias was also higher in participants who had attained up to tertiary education – 75% (27/36) than those who had acquired lower education. Furthermore, considering the clinical factors, participants who had high fasting blood sugar levels ( $\geq$ 120 mg/dl) had more dyslipidemias– 75% (9/12) than those who had normal blood sugar levels (Table 2).

**Table 2:** Prevalence of dyslipidemias according to social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Dyslipidemias Present	No Dyslipidemias	Prevalence Ratio (95% CI)	P-Value
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	No. (%)	No. (%)		
<b>Overall prevalence of dyslipidemias</b>	243 (63.3)	141 (36.7)	58.4 – 68.1	
<b>Age</b> (Categorised at the median)				
18 – 28	128 (59.5)	87 (40.5)		
29 – 49	115 (68.0)	54 (32.0)	1.00	
Median = 28 (18 – 49)			1.14 (0.98 – 1.32)	<b>0.083</b>
<b>Education</b>				
No formal education	6 (42.9)	8 (57.1)	0.68 (0.37 – 1.25)	<b>0.210</b>
Primary	66 (61.7)	41 (38.3)	0.97 (0.81 – 1.16)	<b>0.759</b>
Secondary	144 (63.4)	83 (36.6)	1.00	
Tertiary	27 (75.0)	9 (25.0)	1.18 (0.96 – 1.46)	<b>0.124</b>
<b>Parity</b>				
0 - 1	59 (59.6)	40 (40.4)	1.00	
≥2	184 (64.6)	101 (35.4)	1.08 (0.90 – 1.30)	0.394
<b>Fasting Blood Sugar</b>				
Normal	234 (62.7)	139 (37.3)	1.00	
High	9 (81.8)	2 (18.2)	1.30 (0.98 – 1.74)	<b>0.072</b>
<b>History of Hypertension</b>				
No	235 (63.5)	135 (36.5)	1.00	
Yes	8 (57.1)	6 (42.9)	0.90 (0.57 – 1.43)	0.653
<b>Body Mass Index</b>				
≤25	138 (56.6)	106 (43.4)	1.00	
>25	105 (75.0)	35 (25.0)	1.33 (1.15 – 1.53)	<b>&lt;0.001</b>
<b>ART Use</b>				
No	186 (60.8)	120 (39.2)	1.00	
Yes	57 (73.1)	21 (26.9)	1.20 (1.02 – 1.41)	<b>0.026</b>
<b>Hormonal Contraceptive Used</b>				
Oral Contraceptives	22 (51.2)	21 (48.8)	1.77 (0.57 – 1.05)	<b>0.100</b>
Injectables	128 (66.3)	65 (33.7)	1.00	
Implants	93 (63.8)	55 (35.2)	0.95 (0.81 – 1.11)	<b>0.508</b>
<b>Duration of use of HC</b>				
<6 months	77 (62.1)	47 (37.9)	1.00	
6 to 11 months	22 (53.7)	19 (45.2)	0.86 (0.63 – 1.19)	0.366
12 or more months	144 (65.8)	75 (33.6)	1.06 (0.90 – 1.25)	0.504

### Factors associated with dyslipidemias

The variables that were found to be significantly associated with dyslipidemias were BMI (PR=1.33, 95% CI: 1.15 – 1.54, p<0.001) and ART use (PR= 1.21, 95% CI: 1.03 – 1.42, p=0.020). These variables were further assessed for interaction between each other and for

confounding with other independent variables; however there was no interaction and the association between dyslipidemias and these variables was not confounded by any other independent variables. Therefore, BMI and ART use were the only independent factors associated with dyslipidemias (Table 3).

**Table 3:** Multivariate analysis of the factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Prevalence Ratio	95% Confidence Interval	P-value
<b>Body Mass Index</b>			
≤25	1.00		
>25	1.33	1.15 – 1.54	<0.001
<b>ART Use</b>			
No	1.00		
Yes	1.21	1.03 – 1.42	0.020

## DISCUSSION

Dyslipidemias were found to be present in more than half of the participants. This high prevalence of dyslipidemias could be an overestimate in the general population because of the differences in these populations; the population in this study had a higher prevalence of ART users (20.3%) than what is reported in the general population (less than 5%),[9] and since ART use is associated with dyslipidemias, the high prevalence could have been as a result of the high percentage on ART. The presence of dyslipidemias in hormonal contraceptive users has been reported by several other studies which found significant changes in the lipid profile levels of hormonal contraceptive users.[8, 12, 14, 15] These changes in the lipid profile levels can be attributed to the lipogenic effect of estrogen in which liver lipogenesis is increased that results in elevated levels of Triglycerides and LDL

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3 levels [16]. Furthermore, the progestin component of hormonal contraceptives increases  
4 hepatic lipase enzyme activity which increases the removal of HDL hence decreasing the  
5 serum HDL levels.[17] These results are however contradicted by a study in a China by Wei  
6 and his colleagues in 2011 which found no significant association between oral contraceptive  
7 use and the risk of dyslipidemias.[18] Wei's study used the same classification of  
8 dyslipidemias with the current study (as the presence of one or more abnormal serum lipid  
9 profile level), so the difference could have arisen from the fact that Wei's study used a case  
10 control design while the current study used a cross sectional design.  
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21 The factors found to be significantly associated with dyslipidemias in women using hormonal  
22 contraceptives were BMI and ART use. Participants who had a BMI greater than 25 were  
23 33% more likely to have dyslipidemias compared to those who had a BMI of 25 or less. This  
24 is in line with the findings from a systematic review conducted by Halperin and his  
25 colleagues in 2011 which reported that differences in average BMI of women in the  
26 individual cohorts explained a portion of the heterogeneity found in HDL-C levels.[7] These  
27 changes can be attributed to the fact that BMI can independently affect lipid profile levels as  
28 reported by several studies which observed a significant association between high BMI and  
29 the occurrence of dyslipidemias.[19, 20] The study by Shamai and his colleagues found a  
30 significant association between BMI and both Triglyceride and HDL levels, which was  
31 explained by insulin resistance.[20]  
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44 ART use was the other factor associated with dyslipidemias in women using hormonal  
45 contraceptives. Women who were using anti-retroviral therapy (ART) were 21% more likely  
46 to have dyslipidemias than those who were not. These findings should however be treated  
47 with caution because of the small numbers who were on anti-retroviral therapy in this study.  
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3 changes in lipid profile levels can be attributed to the fact that different ART regimens have  
4 been reported to independently alter lipid profile levels hence aggravating the presence of  
5 dyslipidemias. A study by Bekolo and his colleagues in 2014 demonstrated a high prevalence  
6 of dyslipidemias in HIV patients on first line anti-retroviral therapy in Cameroon.[10] This  
7 was attributed to the fact that some ART regimens exert distinct alterations in lipid  
8 metabolism hence bringing about dyslipidemias.[11]

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11 Some of the strengths of this study are: This is one of the first studies assessing dyslipidemias  
12 in women using hormonal contraceptives to be carried out in Uganda and this contributes to  
13 further understanding and possibly better management of dyslipidemias in women using  
14 hormonal contraceptives. In addition, standardised approaches were used when carrying out  
15 this study and this permits the study to be replicated in different areas or over time with an  
16 assurance that the results produced will have comparable findings.

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19 We acknowledge the following limitations. The findings of this study may not be  
20 generalisable to all hormonal contraceptive users because the sample is not representative  
21 enough and also because the sampling procedure was non-probability which does not allow  
22 equal opportunity to all women to participate. This study was only a cross sectional study so  
23 a causal relationship cannot be ascertained between hormonal contraceptive use and  
24 dyslipidemias. Since questionnaires were used for data collection, some of the self-reported  
25 information may have been inaccurate or incomplete hence affecting some of the results.  
26  
27 Finally, information on the physical activity and diet of the study participants was not  
28 collected which is deemed important for this study since these variables play a significant  
29 role in changing lipid profile levels.

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32 In conclusion, more than half of the women using hormonal contraceptives have  
33 dyslipidemias and are thus at an increased risk of acquiring cardiovascular diseases.  
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35 Hormonal contraceptive users who had a BMI greater than 25 and / or were on anti-retroviral  
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3 therapy were more likely to have dyslipidemias and this in the long run increases their risk  
4 for cardiovascular disease. We therefore recommend the Uganda Ministry of Health to  
5 formulate policy to better manage women using hormonal contraceptives. The policy should  
6 include checking lipid profile levels prior to initiation of hormonal contraceptive use and also  
7 continued assessment of lipid profiles at regular intervals while using these contraceptives.  
8  
9 The policy should in particular target the high risk group that includes women whose BMIs  
10 are greater than 25 and / or are on ART. We also recommend that future research is done to  
11 replicate the study in different populations and also explore whether the relationship between  
12 dyslipidemias and hormonal contraceptive use is causal.  
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28 **Author contribution:**  
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30  
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33 the study. **Pauline B Kibwika** planned and supervised the study, interpreted results, and  
34 reviewed the manuscript. **James Tumwine** planned the study, contributed in acquisition of  
35 funds, interpreted results and revised the manuscript. **Joan N Kalyango** planned and  
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37 **Nabaasa** planned the study, contributed in analysis and reviewed the manuscript. **Irene**  
38 **Najjingo** planned the study, contributed in analysis and reviewed the manuscript. **Grace S**  
39 **Nabaggala** planned the study, contributed in analysis and reviewed the manuscript. **Francis**  
40 **Olweny** planned the study, contributed in analysis and reviewed the manuscript. **Charles**  
41 **Karamagi** conceptualised, planned and supervised the study, interpreted results and reviewed  
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36 explained.  
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## REFERENCES

1. UNFPA, *Annual Report 2015*.
2. UDHS, *Millennium Development Goal Indicators 2011*.
3. Sabatini, R., R. Cagiano, and T. Rabe, *Adverse Effects of Hormonal Contraception*. J. Reproduktionsmed. Endokrinol 2011. **8**(1): p. 130-156.
4. Gaspard, U., et al., *A randomized study on the influence of oral contraceptives containing ethinylestradiol combined with drospirenone or desogestrel on lipid and lipoprotein metabolism over a period of 13 cycles*. Contraception, 2004. **69**(4): p. 271-8.
5. Schueller, P., et al., *Effects of synthetic progestagens on autonomic tone, neurohormones and C-reactive protein levels in young healthy females in reproductive age*. Int J Cardiol, 2006. **111**(1).
6. UBOS, *Demographic health survey*. 2006.
7. Halperin, I.J., et al., *The association between the combined oral contraceptive pill and insulin resistance, dysglycemia and dyslipidemia in women with polycystic ovary syndrome: a systematic review and meta-analysis of observational studies*. Hum Reprod, 2011. **26**(1): p. 191-201.
8. Berenson, A., Rahman Mahbubur, and W. Gregg, *Effect of injectable and oral contraceptives on serum lipids*. Obstetrics and gynecology, 2009. **114**(4): p. 786-794.
9. USAID, *HIV Care and Treatment* (<http://sustainuganda.org/content/hiv-care-and-treatment>). 2017.
10. Bekolo, C.E., et al., *The lipid profile of HIV-infected patients receiving antiretroviral therapy in a rural Cameroonian population*. BMC Public Health, 2014. **14**(1): p. 236.
11. Souza, S.J., et al., *Lipid profile of HIV-infected patients in relation to antiretroviral therapy: a review*. Rev Assoc Med Bras (1992), 2013. **59**(2): p. 186-98.
12. Asare, G.A., et al., *Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease in a Ghanaian community*. International Journal of Women's Health, 2014. **6**: p. 597-603.

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13. NCEP, *Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)*. *Jama*, 2001. **285**(19): p. 2486-97.
14. Sitruk-Ware RL, Menard J, and R. M, *Comparison of the impact of vaginal and oral administration of combined hormonal contraceptives on hepatic proteins sensitive to estrogen*. 2007. **75**: p. 430–7.
15. Stocco B, et al., *The Effect of Different Contraceptive Drugs on the Lipid Profile of Brazilian Women*. *Pharmaceut Anal Acta*, 2013. **4**(1).
16. Faryal, U.R., S.: Hajra B, *Lipid profile in females of reproductive age group using combined oral contraceptive pills* *Gomal J Med Sci*, 2012. **10**: p. 233-6.
17. Yesmin, F., et al., *Lipid Profile in Oral Contraceptives User Women*. *Dinajpur Med Col J* 2013. **6**(1): p. 54-57.
18. Wei, W., et al., *Dyslipidaemia, combined oral contraceptives use and their interaction on the risk of hypertension in Chinese women*. *Journal of Human Hypertension* 2011. **25**: p. 364–371.
19. Jayaswal, A.A., *Relation of Body Mass Index with Lipid Profile and Blood Pressure in Healthy Females of Lower Socioeconomic Group, In Kosi Region, Bihar*. *Journal of Dental and Medical Sciences* 2013. **10**(1): p. 19-21.
20. Shamai, L., et al., *Association of body mass index and lipid profiles: evaluation of a broad spectrum of body mass index patients including the morbidly obese*. *Obes Surg*, 2011. **21**(1): p. 42-7.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

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<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

## MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	4
2	Hypothesis statement	-
3	Description of study outcome(s)	7
4	Type of exposure or intervention used	4-6
5	Type of study designs used	5-7
6	Study population	6
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	5, Title page
8	Search strategy, including time period included in the synthesis and key words	5, Table 1
9	Effort to include all available studies, including contact with authors	6
10	Databases and registries searched	6
11	Search software used, name and version, including special features used (eg, explosion)	6
12	Use of hand searching (eg, reference lists of obtained articles)	6
13	List of citations located and those excluded, including justification	8, Table 2, Fig 1
14	Method of addressing articles published in languages other than English	-
15	Method of handling abstracts and unpublished studies	6
16	Description of any contact with authors	6
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	6-8
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	6-8
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	6-8
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	7
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	6-7
22	Assessment of heterogeneity	7
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	7-8
24	Provision of appropriate tables and graphics	Tables 2-7, Figs 2-7
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figs 3-7
26	Table giving descriptive information for each study included	Table 2
27	Results of sensitivity testing (eg, subgroup analysis)	Fig 3, Table 3
28	Indication of statistical uncertainty of findings	12-16

Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	12, Fig 2
30	Justification for exclusion (eg, exclusion of non-English language citations)	6
31	Assessment of quality of included studies	6-7
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	17-19
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	20
34	Guidelines for future research	-
35	Disclosure of funding source	20

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

# BMJ Open

## Dyslipidemias in women using hormonal contraceptives: a cross sectional study in Mulago Hospital Family Planning Clinic, Kampala

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Keywords:	Hormonal contraceptives, Contraception, Dyslipidemias, Lipid profile

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3 **Dyslipidemias in women using hormonal contraceptives: a cross sectional**  
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5 **study in Mulago Hospital Family Planning Clinic, Kampala**  
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10 Ritah Bakesiima<sup>1</sup>, Pauline Byakika-Kibwika<sup>2</sup>, James Tumwine<sup>3</sup>, Joan N Kalyango<sup>1</sup>, Gloria  
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12 Nabaasa<sup>1</sup>, Irene Najjingo<sup>1</sup>, Grace S Nabaggala<sup>1</sup>, Francis Olweny<sup>1</sup>, Charles Karamagi<sup>3</sup>  
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15  
16 <sup>1</sup>Clinical Epidemiology Unit, School of Medicine, College of Health Sciences, Makerere  
17  
18 University, Kampala, Uganda  
19

20  
21 <sup>2</sup>Department of Internal Medicine, School of Medicine, College of Health Sciences, Makerere  
22  
23 University, Kampala, Uganda  
24

25  
26 <sup>3</sup>Department of Paediatrics, School of Medicine, College of Health Sciences, Makerere  
27  
28 University, Kampala, Uganda  
29

30  
31 Corresponding author: Ritah Bakesiima  
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33  
34 (E-mail: [esmie.ritah@gmail.com](mailto:esmie.ritah@gmail.com))  
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**ABSTRACT**

**Objective:** The aim of this study was to determine the prevalence and factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala.

**Design:** Cross sectional study

**Setting:** Mulago Hospital, Kampala

**Participants:** Three hundred eighty four women aged 18 to 49 years who had used hormonal contraceptives for atleast three months and consented to participate in the study were included in the study.

**Study outcome:** Dyslipidemias defined as derangements in lipid profile levels which included total cholesterol levels  $\geq 200$  mg/dL, high-density lipoprotein levels  $< 40$  mg/dL, triglyceride levels  $> 150$  mg/dL, or low-density lipoprotein levels  $\geq 160$  mg/dL for which the prevalence and associated factors were obtained.

**Results:** The prevalence of dyslipidemias was 63.3% (95% CI: 58.4 – 68.1). Body Mass Index (BMI) (PR=1.33, 95% CI: 1.15-1.54,  $p < 0.001$ ) and use of anti-retroviral therapy (ART) (PR=1.21, 95% CI: 1.03-1.42,  $p = 0.020$ ) were the factors found to be significantly associated with dyslipidemias.

**Conclusion:** Dyslipidemias were present in more than half of the participants and this increases their risk for cardiovascular diseases. The high risk groups were women with a BMI greater than 25 and women who were on ART. Lipid profiles should therefore be assessed in women using hormonal contraceptives in order to manage them better.

**Keywords:** Hormonal Contraceptives, Contraception, Dyslipidemias, Lipid profile

### Strengths and limitations of the study

- i) This being one of the first studies in Uganda to assess dyslipidemias in women using hormonal contraceptives, the cross sectional study design used was the most appropriate to provide baseline information.
- ii) Standard approaches were used to carry out the study to ensure repeatability and reproducibility.
- iii) The selection procedure used was non-probability so results may not be generalisable to all hormonal contraceptive users.
- iv) Since this was a cross-sectional study, a causal relationship between hormonal contraceptive use and dyslipidemias could not be ascertained.
- v) The results may have been subject to information bias because questionnaires were used to obtain information on some variables which are based on recall.

### INTRODUCTION

Globally, the use of contraception has risen slightly, from 54.7% in 1990 to 64% in 2015 [1] and in Uganda particularly, the Contraceptive Prevalence Rate (CPR) is currently at 27.2% with hormonal contraceptives (HCs) accounting for 77.9% of the total contraceptive use.[1] HCs are the most commonly used contraception methods in Uganda, the injectables being the most common at a rate of 72.8%, followed by the oral contraceptive at 14.3%, and finally the implants at 12.9%.[2]

Several researchers have reported the complications and side-effects associated with the use of these hormonal contraceptives which include nausea and vomiting, headaches, dizziness, breast tenderness and enlargement, irregular bleeding or bleeding between periods, and weight gain as the side effects and adverse effects like metabolism impairment, heart and circulation complications, venous thromboembolism, an increased risk of cancer, and liver

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3 problems.[3] It has been suggested that some of the aforementioned complications are a  
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5 consequence of dyslipidemias, a potential metabolic impairment effect of long term use of  
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7 some of these hormonal contraceptives.[4] Furthermore, a study by Schueller and his  
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9 colleagues suggested that these dyslipidemias could also rise as a result of these hormones  
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11 increasing apolipoprotein B-100 synthesis which subsequently increases triglyceride and  
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13 LDL levels.[5]

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15 Several factors have been reported to predispose hormonal contraceptive users to  
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17 dyslipidemias like age, race, body weight, lifestyle, use of other medications like ART,  
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19 steroids and pre-existing diseases like hypertension, diabetes mellitus and obesity.[6-10]

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21 Many of these factors are common in Uganda. For example, 16% of the females in Uganda  
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23 were found to be obese.[11] Obesity is associated with alterations in lipid profile levels, and  
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25 this, in the presence of hormonal contraceptive use increases the risk of dyslipidemias.[7, 8]

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27 In addition, an estimated 39,000 women in Uganda were reported to be on anti-retroviral  
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29 therapy (ART) between June 2010 and March 2017.[12] Some of these antiretroviral drugs  
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31 alter lipid profile levels hence bringing about dyslipidemias.[13, 14]

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33 Poorly managed dyslipidemias can result into cardiovascular diseases like venous  
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35 thromboembolism, myocardial infarction and stroke.[15] However, lipid profile levels are not  
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37 measured in women using hormonal contraceptives in Uganda because little is known about  
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39 the dyslipidemic effect of hormonal contraceptives. This study therefore aimed at  
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41 determining the prevalence and factors associated with dyslipidemias in women using  
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43 hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala.  
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## METHODS

### **Study design, setting and population**

This was a cross sectional study employing both descriptive and analytical techniques carried out from Mulago Hospital Family Planning Clinic, Kampala in March and April, 2017. The family planning clinic of Mulago Hospital receives approximately 320 patients monthly, 215 of whom are hormonal contraceptive users. Using the consecutive sampling procedure, a total of 384 women aged 18 to 49 years who had used hormonal contraceptives for atleast three months and consented to participate in the study were included in the study, and all women who were unable to comprehend either English or Luganda and could not adhere to study procedures were excluded from the study. For ethical considerations, necessary permission to carry out this study was obtained from the School of Medicine Research and Ethics Committee, the Uganda National Counsel of Science and Technology and Mulago Hospital. Written informed consent was obtained from all the participants before enrolment into the study and confidentiality was highly maintained.

### **Data collection**

A questionnaire was administered to collect basic information on age, parity, highest level of education, occupation, type of hormonal contraceptive used, duration of use of hormonal contraceptives, use of anti-retroviral drugs and history of hypertension. Body Mass Index (BMI) was determined by measuring weight using the Seca weighing scale and height using a stadiometer. BMI was then computed as Weight (in Kg)/Height (in metres squared). Blood samples were aseptically collected from participants after a 6 hour fast and placed in a red top vacutainer without an anticoagulant for the determination of lipid profile levels. The collected samples were allowed to clot for atleast 3 minutes and centrifuged at 2400rev/min for 5minutes. The serum obtained from centrifugation was pipetted into Cobas 6000 caps and taken for analysis using the Cobas 6000 chemistry analyzer. Fasting blood sugar levels were

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3 determined using a Freestyle glucometer for all the participants six hours after their last meal.  
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5 A sterile single use lancet was used to puncture the participant's disinfected fingure and a  
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7 small drop of the blood placed onto the glucometer strip already mounted into the  
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9 glucometer. The blood sugar level was read off and recorded in mg/dl.  
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### 11 12 **Outcome variable**

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14 The outcome variable for this study was dyslipidemias defined as derangements in the lipid  
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16 profile levels which included a total cholesterol level of 200 mg/dL or greater, a high-density  
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18 lipoprotein cholesterol level of less than 40 mg/dL, a triglyceride level of greater than 150  
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20 mg/dL, or a low-density lipoprotein cholesterol level of 160 mg/dL or greater according to  
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22 the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III)  
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24 guidelines.[16] A participant was said to have dyslipidemias if they had any of the lipid  
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26 profile parameters in ranges stated above. The presence of dyslipidemias was coded as "1"  
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28 and its absence as "0".  
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### 31 32 **Statistical analysis**

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34 Data were analysed using STATA version 13.0 in which all continuous variables were  
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36 summarised as medians and ranges while the categorical variables were summarised as  
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38 percentages and proportions. The prevalence of dyslipidemias was calculated as the  
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40 percentage of women with dyslipidemias over the total number of women in the study. The  
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42 modified Poisson regression model was used to analyse the factors associated with  
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44 dyslipidemias in women using hormonal contraceptives. In the multivariate analysis,  
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46 variables which were found to be significantly associated with dyslipidemias ( $p < 0.05$ ) were  
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48 used to form two-way product terms which were used in the assessment of interaction using  
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50 the chunk test. Where necessary, confounding was assessed for. Confounders were retained  
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52 only if they changed the estimates by greater than or equal to 10%. Confidence intervals were  
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3 presented at 95% level of significance along with the p-values. Statistical significance was  
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5 considered at a p-value of less than or equal to 0.05.  
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### 8 **Patient and public involvement**

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10 Due to patients' experiences and complaints raised by most of the patients that they gained  
11 weight while using hormonal contraceptives, we felt the need to determine whether long term  
12 use of hormonal contraceptives has an effect on lipid profile levels as well. This way, patient  
13 experiences informed our research questions and study outcomes.  
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17 Patients were involved in the design of the study by informing the design of the data  
18 collection tool. This was majorly during the pre-testing or piloting of the questionnaires,  
19 however patients were not involved in the recruitment to or the conduct of the study.  
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25 Results will be disseminated to study participants through the use of text messages and fliers  
26 that will be issued out at the family planning clinic printed both in English and Luganda.  
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## 31 **RESULTS**

### 32 **Participants' characteristics**

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34 The median age of the 384 participants was 28 years (IQR: 18 – 49). An estimated 59.1%  
35 (227/384) of the participants had attained only up to secondary education, 74.2% (285/384)  
36 had at least two or more children and 39.6% (152/384) were self-employed. Only 11 (2.9%)  
37 had high fasting blood sugar levels ( $\geq 120$  mg/dl), 14 (3.7%) had a history of hypertension,  
38 140 (36.5%) had a BMI  $>25$  and 78 (20.3%) were on anti-retroviral therapy (ART). Most of  
39 the participants were using Progestin-Only Injectables - 185 (48.2%) and 219 (57.0%) had  
40 used hormonal contraceptives for over a year (Table 1).  
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**Table 1:** Social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Number (N=384)	Percentage (%)
<b>Age</b> (Categorised at the median)		
18 – 28	215	56.0
29 – 49	169	44.0
Median (IQR): 28 (18 – 49)		
<b>Education</b>		
No formal education	14	3.6
Primary	107	27.9
Secondary	227	59.1
Tertiary	36	9.4
<b>Parity</b>		
0 - 1	99	25.8
Two or more	285	74.2
<b>Fasting Blood Sugar</b>		
Normal (<120 mg/dl)	373	97.1
High (≥120 mg/dl)	11	2.9
<b>History of Hypertension</b>		
No	370	96.3
Yes	14	3.7
<b>Body Mass Index (BMI)</b>		
≤25	244	63.5
>25	140	36.5
<b>ART Use</b>		
No	306	79.7
Yes	78	20.3
<b>Hormonal Contraceptive Used</b>		
Progestin Only Pill (POP)	5	1.3
Combined Oral Pill (COP)	38	9.9
Progestin Only Injectable (POI)	185	48.2
Combined Injectable Contraceptive (CIC)	8	2.1
Implant (1 rod)	124	32.3
Implant (2 rods)	24	6.2
<b>Duration of use of HC</b>		
<6 months	124	32.3
6 to 11 months	41	10.7
12 or more months	219	57.0

### Prevalence of dyslipidemias

The prevalence of dyslipidemias amongst the 384 participants was 63.3% (95% CI: 58.4 – 68.1). Dyslipidemias were higher in women aged above 28 years at 68.0% (115/169) compared to those who were younger. The prevalence of dyslipidemias was also higher in

participants who had attained up to tertiary education at 75% (27/36) than those who had acquired lower education. Furthermore, considering the clinical factors, participants who had high fasting blood sugar levels ( $\geq 120$  mg/dl) had more dyslipidemias at 81.8% (9/11) than those who had normal blood sugar levels (Table 2).

**Table 2:** Prevalence of dyslipidemias according to social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Dyslipidemias Present No. (%)	No Dyslipidemias No. (%)	Prevalence Ratio (95% CI)	P-Value
<b>Overall prevalence of dyslipidemias</b>	243 (63.3)	141 (36.7)	58.4 – 68.1	
<b>Age</b> (Categorised at the median)				
18 – 28	128 (59.5)	87 (40.5)	1.00	
29 – 49	115 (68.0)	54 (32.0)	1.14(0.98-1.32)	<b>0.083</b>
Median = 28 (18 – 49)				
<b>Education</b>				
No formal education	6 (42.9)	8 (57.1)	0.68 (0.37 – 1.25)	<b>0.210</b>
Primary	66 (61.7)	41 (38.3)	0.97 (0.81 – 1.16)	<b>0.759</b>
Secondary	144 (63.4)	83 (36.6)	1.00	
Tertiary	27 (75.0)	9 (25.0)	1.18 (0.96 – 1.46)	<b>0.124</b>
<b>Parity</b>				
0 - 1	59 (59.6)	40 (40.4)	1.00	
$\geq 2$	184 (64.6)	101 (35.4)	1.08 (0.90 – 1.30)	0.394
<b>Fasting Blood Sugar</b>				
Normal	234 (62.7)	139 (37.3)	1.00	
High	9 (81.8)	2 (18.2)	1.30 (0.98 – 1.74)	<b>0.072</b>
<b>History of Hypertension</b>				
No	235 (63.5)	135 (36.5)	1.00	
Yes	8 (57.1)	6 (42.9)	0.90 (0.57 – 1.43)	0.653
<b>Body Mass Index</b>				
$\leq 25$	138 (56.6)	106 (43.4)	1.00	
$> 25$	105 (75.0)	35 (25.0)	1.33 (1.15 – 1.53)	<b>&lt;0.001</b>
<b>ART Use</b>				
No	186 (60.8)	120 (39.2)	1.00	
Yes	57 (73.1)	21 (26.9)	1.20 (1.02 – 1.41)	<b>0.026</b>
<b>Hormonal Contraceptive Used</b>				

Oral Contraceptives	22 (51.2)	21 (48.8)	1.77 (0.57 – 1.05)	<b>0.100</b>
Injectables	128 (66.3)	65 (33.7)	1.00	
Implants	93 (63.8)	55 (35.2)	0.95 (0.81 – 1.11)	<b>0.508</b>
<b>Duration of use of HC</b>				
<6 months	77 (62.1)	47 (37.9)	1.00	
6 to 11 months	22 (53.7)	19 (45.2)	0.86 (0.63 – 1.19)	0.366
12 or more months	144 (65.8)	75 (33.6)	1.06 (0.90 – 1.25)	0.504

### Factors associated with dyslipidemias

The variables that were found to be significantly associated with dyslipidemias were BMI (PR=1.33, 95% CI: 1.15 – 1.54,  $p<0.001$ ) and ART use (PR= 1.21, 95% CI: 1.03 – 1.42,  $p=0.020$ ). These variables were further assessed for interaction between each other and for confounding with other independent variables; however there was no interaction and the association between dyslipidemias and these variables was not confounded by any other independent variables. Therefore, BMI and ART use were the only independent factors associated with dyslipidemias (Table 3).

**Table 3:** Multivariate analysis of the factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Prevalence Ratio	95% Confidence Interval	P-value
<b>Body Mass Index</b>			
≤25	1.00		
>25	1.33	1.15 – 1.54	<0.001
<b>ART Use</b>			
No	1.00		
Yes	1.21	1.03 – 1.42	0.020

## DISCUSSION

Dyslipidemias were found to be present in more than half of the participants. This high prevalence of dyslipidemias could be an overestimate in the general population because of the differences in these populations; the population in this study had a higher prevalence of ART users (20.3%) than what is reported in the general population (less than 5%),[12] and since ART use is associated with dyslipidemias, the high prevalence could have been as a result of the high percentage on ART. The presence of dyslipidemias in hormonal contraceptive users has been reported by several other studies which found significant changes in the lipid profile levels of hormonal contraceptive users.[7, 15, 17, 18] These changes in the lipid profile levels can be attributed to the lipogenic effect of estrogen in which liver lipogenesis is increased that results in elevated levels of Triglycerides and LDL levels [19]. Furthermore, the progestin component of hormonal contraceptives increases hepatic lipase enzyme activity which increases the removal of HDL hence decreasing the serum HDL levels.[20] These results are however contradicted by a study in China by Wei and his colleagues in 2011 which found no significant association between oral contraceptive use and the risk of dyslipidemias.[10] Wei's study used the same classification of dyslipidemias with the current study (as the presence of one or more abnormal serum lipid profile level), so the difference could have arisen from the fact that Wei's study used a case control design while the current study used a cross sectional design.

The factors found to be significantly associated with dyslipidemias in women using hormonal contraceptives were BMI and ART use. Participants who had a BMI greater than 25 were 33% more likely to have dyslipidemias compared to those who had a BMI of 25 or less. This is in line with the findings from a systematic review conducted by Halperin and his colleagues in 2011 which reported that differences in average BMI of women in the

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3 individual cohorts explained a portion of the heterogeneity found in HDL-C levels.[8] These  
4 changes can be attributed to the fact that BMI can independently affect lipid profile levels as  
5 reported by several studies which observed a significant association between high BMI and  
6 the occurrence of dyslipidemias.[21, 22] The study by Shamai and his colleagues found a  
7 significant association between BMI and both Triglyceride and HDL levels, which was  
8 explained by insulin resistance.[22]

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16 ART use was the other factor associated with dyslipidemias in women using hormonal  
17 contraceptives. Women who were using anti-retroviral therapy (ART) were 21% more likely  
18 to have dyslipidemias than those who were not. These findings should however be treated  
19 with caution because of the small numbers who were on anti-retroviral therapy in this study.  
20 This is one of the first studies to report on dyslipidemias in ART users on hormonal  
21 contraceptives; therefore there are no comparative study findings to use. These changes in  
22 lipid profile levels can be attributed to the fact that different ART regimens have been  
23 reported to independently alter lipid profile levels hence aggravating the presence of  
24 dyslipidemias. A study by Bekolo and his colleagues in 2014 demonstrated a high prevalence  
25 of dyslipidemias in HIV patients on first line anti-retroviral therapy in Cameroon.[13] This  
26 was attributed to the fact that some ART regimens exert distinct alterations in lipid  
27 metabolism hence bringing about dyslipidemias.[14]

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42 Some of the strengths of this study are: This is one of the first studies assessing dyslipidemias  
43 in women using hormonal contraceptives to be carried out in Uganda and this contributes to  
44 further understanding and possibly better management of dyslipidemias in women using  
45 hormonal contraceptives. In addition, standardised approaches were used when carrying out  
46 this study and this permits the study to be replicated in different areas or over time with an  
47 assurance that the results produced will have comparable findings.  
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3 We acknowledge the following limitations. The findings of this study may not be  
4 generalisable to all hormonal contraceptive users because the sample is not representative  
5 enough and also because the sampling procedure was non-probability which does not allow  
6 equal opportunity to all women to participate. This study was only a cross sectional study so  
7 a causal relationship cannot be ascertained between hormonal contraceptive use and  
8 dyslipidemias. Since questionnaires were used for data collection, some of the self-reported  
9 information may have been inaccurate or incomplete hence affecting some of the results.  
10 Finally, information on the physical activity and diet of the study participants was not  
11 collected which is deemed important for this study since these variables play a significant  
12 role in changing lipid profile levels.  
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15 In conclusion, more than half of the women using hormonal contraceptives have  
16 dyslipidemias and are thus at an increased risk of acquiring cardiovascular diseases.  
17 Hormonal contraceptive users who had a BMI greater than 25 and / or were on anti-retroviral  
18 therapy were more likely to have dyslipidemias and this in the long run increases their risk  
19 for cardiovascular disease. We therefore recommend the Uganda Ministry of Health to  
20 formulate policy to better manage women using hormonal contraceptives. The policy should  
21 include checking lipid profile levels prior to initiation of hormonal contraceptive use and also  
22 continued assessment of lipid profiles at regular intervals while using these contraceptives.  
23 The policy should in particular target the high risk group that includes women whose BMIs  
24 are greater than 25 and / or are on ART. We also recommend that future research is done to  
25 replicate the study in different populations and also explore whether the relationship between  
26 dyslipidemias and hormonal contraceptive use is causal.  
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**Author contribution:**

**Ritah Bakesiima** conceptualised the study, designed it, planned the analysis, did the result interpretation and wrote the manuscript. She is the guarantor and responsible investigator of the study. **Pauline B Kibwika** planned and supervised the study, interpreted results, and reviewed the manuscript. **James Tumwine** planned the study, contributed in acquisition of funds, interpreted results and revised the manuscript. **Joan N Kalyango** planned and supervised the study and analysis, interpreted results, and revised the manuscript. **Gloria Nabaasa** planned the study, contributed in analysis and reviewed the manuscript. **Irene Najjingo** planned the study, contributed in analysis and reviewed the manuscript. **Grace S Nabaggala** planned the study, contributed in analysis and reviewed the manuscript. **Francis Olweny** planned the study, contributed in analysis and reviewed the manuscript. **Charles Karamagi** conceptualised, planned and supervised the study, interpreted results and reviewed the manuscript.

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11 *the study have been omitted; and that any discrepancies from the study as planned have been*  
12 *explained.*  
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18 **Data sharing:** All available data can be obtained by contacting the corresponding author.  
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## 24 REFERENCES

- 25  
26 1. UNFPA, *Annual Report* (<http://www.unfpa.org/annual-report-2015>). 2015.  
27 2. UDHS, *Millennium Development Goal Indicators* (<http://www.ubos.org/onlinefiles/uploads/ubos/UDHS/UDHS2011.pdf>). 2011.  
28 3. Sabatini, R., R. Cagiano, and T. Rabe, *Adverse Effects of Hormonal Contraception*. *J. Reproduktionsmed. Endokrinol* 2011. **8**(1): p. 130-156.  
29 4. Gaspard, U., et al., *A randomized study on the influence of oral contraceptives containing*  
30 *ethinylestradiol combined with drospirenone or desogestrel on lipid and lipoprotein*  
31 *metabolism over a period of 13 cycles*. *Contraception*, 2004. **69**(4): p. 271-8.  
32 5. Schueller, P., et al., *Effects of synthetic progestagens on autonomic tone, neurohormones*  
33 *and C-reactive protein levels in young healthy females in reproductive age*. *Int J Cardiol*,  
34 2006. **111**(1).  
35 6. Abdel-Barry, J.A., et al., *Lipoprotein changes in women taking low-dose combined oral*  
36 *contraceptive pills: a cross-sectional study in Basra, Iraq*. *EMHJ*, 2011. **17**(9).  
37 7. Berenson, A., Rahman Mahbubur, and W. Gregg, *Effect of injectable and oral contraceptives*  
38 *on serum lipids*. *Obstetrics and gynecology*, 2009. **114**(4): p. 786-794.  
39 8. Halperin, I.J., et al., *The association between the combined oral contraceptive pill and insulin*  
40 *resistance, dysglycemia and dyslipidemia in women with polycystic ovary syndrome: a*  
41 *systematic review and meta-analysis of observational studies*. *Hum Reprod*, 2011. **26**(1): p.  
42 191-201.  
43 9. Okeke, U., et al., *Comparative Effects of Injectable and Oral Hormonal Contraceptives on*  
44 *Lipid Profile*. *European Journal of Medicine*, 2011. **2**(1).  
45 10. Wei, W., et al., *Dyslipidaemia, combined oral contraceptives use and their interaction on the*  
46 *risk of hypertension in Chinese women*. *Journal of Human Hypertension* 2011. **25**: p. 364–  
47 371.  
48 11. UBOS, *Uganda demographic and health survey* (<https://dhsprogram.com/pubs/pdf/FR264/FR264.pdf>). 2011.  
49 12. USAID, *HIV Care and Treatment* (<http://sustainuganda.org/content/hiv-care-and-treatment>).  
50 2017.  
51 13. Bekolo, C.E., et al., *The lipid profile of HIV-infected patients receiving antiretroviral therapy in*  
52 *a rural Cameroonian population*. *BMC Public Health*, 2014. **14**(1): p. 236.  
53  
54  
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57  
58  
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60

14. Souza, S.J., et al., *Lipid profile of HIV-infected patients in relation to antiretroviral therapy: a review*. Rev Assoc Med Bras (1992), 2013. **59**(2): p. 186-98.
15. Asare, G.A., et al., *Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease in a Ghanaian community*. International Journal of Women's Health, 2014. **6**: p. 597-603.
16. NCEP, *Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)*. Jama, 2001. **285**(19): p. 2486-97.
17. Sitruk-Ware, R., Menard J, and R. M, *Comparison of the impact of vaginal and oral administration of combined hormonal contraceptives on hepatic proteins sensitive to estrogen*. 2007. **75**: p. 430-7.
18. Stocco, B., Fumagalli HF, , et al., *The Effect of Different Contraceptive Drugs on the Lipid Profile of Brazilian Women*. Pharmaceut Anal Acta, 2013. **4**(1).
19. Faryal, U.R., S.: Hajra B, *Lipid profile in females of reproductive age group using combined oral contraceptive pills* Gomol J Med Sci, 2012. **10**: p. 233-6.
20. Yesmin, F., et al., *Lipid Profile in Oral Contraceptives User Women*. Dinajpur Med Col J 2013. **6**(1): p. 54-57.
21. Jayaswal, A.A., *Relation of Body Mass Index with Lipid Profile and Blood Pressure in Healthy Females of Lower Socioeconomic Group, In Kosi Region, Bihar*. Journal of Dental and Medical Sciences 2013. **10**(1): p. 19-21.
22. Shamai, L., et al., *Association of body mass index and lipid profiles: evaluation of a broad spectrum of body mass index patients including the morbidly obese*. Obes Surg, 2011. **21**(1): p. 42-7.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Reported on Page No.
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 - 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 - 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 - 6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 - 6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	-
		(d) If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	-
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7 - 8 and Table 1
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	9 - 10 and

Table 2

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(b) Report category boundaries when continuous variables were categorized	8 – 9, Table 1 and 2
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	2 and 13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11 – 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Dyslipidemias in women using hormonal contraceptives: a cross sectional study in Mulago Hospital Family Planning Clinic, Kampala

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Keywords:	Hormonal contraceptives, Contraception, Dyslipidemias, Lipid profile

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3 **Dyslipidemias in women using hormonal contraceptives: a cross sectional**  
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10 Ritah Bakesiima<sup>1</sup>, Pauline Byakika-Kibwika<sup>2</sup>, James Tumwine<sup>3</sup>, Joan N Kalyango<sup>1</sup>, Gloria  
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12 Nabaasa<sup>1</sup>, Irene Najjingo<sup>1</sup>, Grace S Nabaggala<sup>1</sup>, Francis Olweny<sup>1</sup>, Charles Karamagi<sup>3</sup>  
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15  
16 <sup>1</sup>Clinical Epidemiology Unit, School of Medicine, College of Health Sciences, Makerere  
17  
18 University, Kampala, Uganda  
19

20  
21 <sup>2</sup>Department of Internal Medicine, School of Medicine, College of Health Sciences, Makerere  
22  
23 University, Kampala, Uganda  
24

25  
26 <sup>3</sup>Department of Paediatrics, School of Medicine, College of Health Sciences, Makerere  
27  
28 University, Kampala, Uganda  
29

30  
31 Corresponding author: Ritah Bakesiima  
32

33  
34 (E-mail: [esmie.ritah@gmail.com](mailto:esmie.ritah@gmail.com))  
35

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37 +256772029182, +256706807057  
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**ABSTRACT**

**Objective:** The aim of this study was to determine the prevalence and factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala.

**Design:** Cross sectional study

**Setting:** Mulago Hospital, Kampala

**Participants:** Three hundred and eighty four women aged 18 to 49 years who had used hormonal contraceptives for atleast three months prior to the study and consented to participate in the study were included in the study.

**Study outcome:** Dyslipidemias defined as derangements in lipid profile levels which included total cholesterol levels  $\geq 200$  mg/dL, high-density lipoprotein levels  $< 40$  mg/dL, triglyceride levels  $> 150$  mg/dL, or low-density lipoprotein levels  $\geq 160$  mg/dL for which the prevalence and associated factors were obtained.

**Results:** The prevalence of dyslipidemias was 63.3% (95% CI: 58.4 – 68.1). Body Mass Index (BMI) (PR=1.33, 95% CI: 1.15-1.54,  $p < 0.001$ ) and use of anti-retroviral therapy (ART) (PR=1.21, 95% CI: 1.03-1.42,  $p = 0.020$ ) were the factors found to be significantly associated with dyslipidemias.

**Conclusion:** Dyslipidemias were present in more than half of the participants and this increases their risk for cardiovascular diseases. The high risk groups were women with a BMI greater than 25 and women who were on ART. Lipid profiles should therefore be assessed in women using hormonal contraceptives in order to manage them better.

**Keywords:** Hormonal Contraceptives, Contraception, Dyslipidemias, Lipid profile

### Strengths and limitations of the study

- i) This being one of the first studies in Uganda to assess dyslipidemias in women using hormonal contraceptives, the cross sectional study design used was the most appropriate to provide baseline information.
- ii) Standard approaches were used to carry out the study to ensure repeatability and reproducibility.
- iii) The selection procedure used was non-probability so results may not be generalisable to all hormonal contraceptive users.
- iv) Since this was a cross-sectional study, a causal relationship between hormonal contraceptive use and dyslipidemias could not be ascertained.
- v) The results may have been subject to information bias because questionnaires were used to obtain information on some variables which are based on recall.

### INTRODUCTION

Globally, the use of contraception has risen slightly, from 54.7% in 1990 to 64% in 2015 [1] and in Uganda particularly, the Contraceptive Prevalence Rate (CPR) is currently at 27.2% with hormonal contraceptives (HCs) accounting for 77.9% of the total contraceptive use.[1] HC's are the most commonly used contraception methods in Uganda, the injectables being the most common at a rate of 72.8%, followed by the oral contraceptive at 14.3%, and finally the implants at 12.9%.[2]

Several researchers have reported the complications and side-effects associated with the use of these hormonal contraceptives which include nausea and vomiting, headaches, dizziness, breast tenderness and enlargement, irregular bleeding or bleeding between periods, and weight gain as the side effects and adverse effects like metabolism impairment, heart and circulation complications, venous thromboembolism, an increased risk of cancer, and liver

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3 problems.[3] It has been suggested that some of the aforementioned complications are a  
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5 consequence of dyslipidemias, a potential metabolic impairment effect of long term use of  
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7 some of these hormonal contraceptives.[4] Furthermore, a study by Schueller and his  
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9 colleagues suggested that these dyslipidemias could also rise as a result of these hormones  
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11 increasing apolipoprotein B-100 synthesis which subsequently increases triglyceride and  
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13 LDL levels.[5]  
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16 Several factors have been reported to predispose hormonal contraceptive users to  
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18 dyslipidemias like age, race, body weight, lifestyle, use of other medications like ART,  
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20 steroids and pre-existing diseases like hypertension, diabetes mellitus and obesity.[6-10]  
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23 Many of these factors are common in Uganda. For example, 16% of the females in Uganda  
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25 were found to be obese.[11] Obesity is associated with alterations in lipid profile levels, and  
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27 this, in the presence of hormonal contraceptive use increases the risk of dyslipidemias.[7, 8]  
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30 In addition, an estimated 39,000 women in Uganda were reported to be on anti-retroviral  
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32 therapy (ART) between June 2010 and March 2017.[12] Some of these antiretroviral drugs  
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34 alter lipid profile levels hence bringing about dyslipidemias.[13, 14]  
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37 Poorly managed dyslipidemias can result into cardiovascular diseases like venous  
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39 thromboembolism, myocardial infarction and stroke.[15] However, lipid profile levels are not  
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41 routinely measured in women using hormonal contraceptives in Uganda because little is  
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43 known about the dyslipidemic effect of hormonal contraceptives. This study therefore aimed  
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45 at determining the prevalence and factors associated with dyslipidemias in women using  
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47 hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala.  
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## METHODS

### Study design, setting and population

This was a cross sectional study employing both descriptive and analytical techniques carried out from Mulago Hospital Family Planning Clinic, Kampala in March and April, 2017. The family planning clinic of Mulago Hospital receives approximately 320 patients monthly, 215 of whom are hormonal contraceptive users. Using the consecutive sampling procedure, a total of 384 women aged 18 to 49 years who had used hormonal contraceptives for atleast three months prior to the study and consented to participate in the study were included in the study, while all women who were unable to comprehend either English or Luganda and were physically or mentally unable to adhere to study procedures like interviews were excluded from the study. For ethical considerations, necessary permission to carry out this study was obtained from the School of Medicine Research and Ethics Committee, the Uganda National Counsel of Science and Technology and Mulago Hospital. Written informed consent was obtained from all the participants before enrolment into the study and confidentiality was highly maintained.

**Sample size calculation:** The Kish Leslie formula was used to estimate the sample size for the prevalence objective, while the formula for comparing means in two proportions by Cummings was used to determine the sample size for the factors associated with dyslipidemias in women using hormonal contraceptives. In both formulas, we considered an error of 0.05, 95% confidence level and power of 80%. We also accounted for 10% missing data in the calculation of the sample size.

### Data collection

A questionnaire was administered to collect basic information on age, parity, highest level of education, occupation, type of hormonal contraceptive used, duration of use of hormonal contraceptives, use of anti-retroviral drugs and history of hypertension. Body Mass Index

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3 (BMI) was determined by measuring weight using the Seca weighing scale and height using a  
4 stadiometer. BMI was then computed as Weight (in Kg)/Height (in metres squared). Blood  
5 samples were aseptically collected from participants after a 6 hour fast and placed in a red top  
6 vacutainer without an anticoagulant for the determination of lipid profile levels. The collected  
7 samples were allowed to clot for atleast 3 minutes and centrifuged at 2400rev/min for  
8 5minutes. The serum obtained from centrifugation was pipetted into Cobas 6000 caps and  
9 taken for analysis using the Cobas 6000 chemistry analyzer. Fasting blood sugar levels were  
10 determined using a Freestyle glucometer for all the participants six hours after their last meal.  
11 A sterile single use lancet was used to puncture the participant's disinfected fingure and a  
12 small drop of the blood placed onto the glucometer strip already mounted into the  
13 glucometer. The blood sugar level was read off and recorded in mg/dl.  
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### 27 **Outcome variable**

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29 The outcome variable for this study was dyslipidemias defined as derangements in the lipid  
30 profile levels which included a total cholesterol level of 200 mg/dL or greater, a high-density  
31 lipoprotein cholesterol level of less than 40 mg/dL, a triglyceride level of greater than 150  
32 mg/dL, or a low-density lipoprotein cholesterol level of 160 mg/dL or greater according to  
33 the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III)  
34 guidelines.[16] A participant was said to have dyslipidemias if they had any of the lipid  
35 profile parameters in ranges stated above. The presence of dyslipidemias was coded as "1"  
36 and its absence as "0".  
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### 48 **Statistical analysis**

49 Data were analysed using STATA version 13.0 in which all continuous variables were  
50 summarised as medians and ranges while the categorical variables were summarised as  
51 percentages and proportions. The prevalence of dyslipidemias was calculated as the  
52 percentage of women with dyslipidemias over the total number of women in the study. The  
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3 modified Poisson regression model was used to analyse the factors associated with  
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5 dyslipidemias in women using hormonal contraceptives. In the multivariate analysis,  
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7 variables which were found to be significantly associated with dyslipidemias ( $p < 0.05$ ) were  
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9 used to form two-way product terms which were used in the assessment of interaction using  
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11 the chunk test. Where necessary, confounding was assessed for. Confounders were retained  
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13 only if they changed the estimates by greater than or equal to 10%. Confidence intervals were  
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15 presented at 95% level of significance along with the p-values. Statistical significance was  
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17 considered at a p-value of less than or equal to 0.05.  
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### 20 21 **Patient and public involvement**

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23 Due to patients' experiences and complaints raised by most of the patients that they gained  
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25 weight while using hormonal contraceptives, we felt the need to determine whether long term  
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27 use of hormonal contraceptives has an effect on lipid profile levels as well. This way, patient  
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29 experiences informed our research questions and study outcomes.  
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32 Patients were involved in the design of the study by informing the design of the data  
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34 collection tool. This was majorly during the pre-testing or piloting of the questionnaires.  
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36 Results will be disseminated to study participants through the use of text messages and fliers  
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38 that will be issued out at the family planning clinic printed both in English and Luganda.  
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## 43 **RESULTS**

### 44 45 **Participants' characteristics**

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47 The median age of the 384 participants was 28 years (IQR: 18 – 49). An estimated 59.1%  
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49 (227/384) of the participants had attained only up to secondary education, 74.2% (285/384)  
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51 had atleast two or more children and 39.6% (152/384) were self-employed. Only 11 (2.9%)  
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53 had high fasting blood sugar levels ( $\geq 120$  mg/dl), 14 (3.7%) had a history of hypertension,  
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55 140 (36.5%) had a BMI  $> 25$  and 78 (20.3%) were on anti-retroviral therapy (ART). Most of  
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the participants were using Progestin-Only Injectables - 185 (48.2%) and 219 (57.0%) had used hormonal contraceptives for over a year (Table 1).

**Table 1:** Social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Number (N=384)	Percentage (%)
<b>Age</b> (Categorised at the median)		
18 – 28	215	56.0
29 – 49	169	44.0
Median (IQR): 28 (18 – 49)		
<b>Education</b>		
No formal education	14	3.6
Primary	107	27.9
Secondary	227	59.1
Tertiary	36	9.4
<b>Parity</b>		
0 - 1	99	25.8
Two or more	285	74.2
<b>Fasting Blood Sugar</b>		
Normal (<120 mg/dl)	373	97.1
High (≥120 mg/dl)	11	2.9
<b>History of Hypertension</b>		
No	370	96.3
Yes	14	3.7
<b>Body Mass Index (BMI)</b>		
≤25	244	63.5
>25	140	36.5
<b>ART Use</b>		
No	306	79.7
Yes	78	20.3
<b>Hormonal Contraceptive Used</b>		
Progestin Only Pill (POP)	5	1.3
Combined Oral Pill (COP)	38	9.9
Progestin Only Injectable (POI)	185	48.2
Combined Injectable Contraceptive (CIC)	8	2.1
Implant (1 rod)	124	32.3
Implant (2 rods)	24	6.2
<b>Duration of use of HC</b>		
<6 months	124	32.3
6 to 11 months	41	10.7
12 or more months	219	57.0

## Prevalence of dyslipidemias

The prevalence of dyslipidemias amongst the 384 participants was 63.3% (95% CI: 58.4 – 68.1). Dyslipidemias were higher in women aged above 28 years at 68.0% (115/169) compared to those who were younger. The prevalence of dyslipidemias was also higher in participants who had attained up to tertiary education at 75% (27/36) than those who had acquired lower education. Furthermore, considering the clinical factors, participants who had high fasting blood sugar levels ( $\geq 120$  mg/dl) had more dyslipidemias at 81.8% (9/11) than those who had normal blood sugar levels (Table 2).

**Table 2:** Prevalence of dyslipidemias according to social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Dyslipidemias Present No. (%)	No Dyslipidemias No. (%)	Prevalence Ratio (95% CI)	P-Value
<b>Overall prevalence of dyslipidemias</b>	243 (63.3)	141 (36.7)	58.4 – 68.1	
<b>Age</b> (Categorised at the median)				
18 – 28	128 (59.5)	87 (40.5)	1.00	
29 – 49	115 (68.0)	54 (32.0)	1.14(0.98-1.32)	<b>0.083</b>
Median = 28 (18 – 49)				
<b>Education</b>				
No formal education	6 (42.9)	8 (57.1)	0.68 (0.37 – 1.25)	<b>0.210</b>
Primary	66 (61.7)	41 (38.3)	0.97 (0.81 – 1.16)	<b>0.759</b>
Secondary	144 (63.4)	83 (36.6)	1.00	
Tertiary	27 (75.0)	9 (25.0)	1.18 (0.96 – 1.46)	<b>0.124</b>
<b>Parity</b>				
0 - 1	59 (59.6)	40 (40.4)	1.00	
$\geq 2$	184 (64.6)	101 (35.4)	1.08 (0.90 – 1.30)	0.394
<b>Fasting Blood Sugar</b>				
Normal	234 (62.7)	139 (37.3)	1.00	
High	9 (81.8)	2 (18.2)	1.30 (0.98 – 1.74)	<b>0.072</b>
<b>History of Hypertension</b>				
No	235 (63.5)	135 (36.5)	1.00	

Yes	8 (57.1)	6 (42.9)	0.90 (0.57 – 1.43)	0.653
<b>Body Mass Index</b>				
≤25	138 (56.6)	106 (43.4)	1.00	
>25	105 (75.0)	35 (25.0)	1.33 (1.15 – 1.53)	<0.001
<b>ART Use</b>				
No	186 (60.8)	120 (39.2)	1.00	
Yes	57 (73.1)	21 (26.9)	1.20 (1.02 – 1.41)	0.026
<b>Hormonal Contraceptive Used</b>				
Oral Contraceptives	22 (51.2)	21 (48.8)	1.77 (0.57 – 1.05)	0.100
Injectables	128 (66.3)	65 (33.7)	1.00	
Implants	93 (63.8)	55 (35.2)	0.95 (0.81 – 1.11)	0.508
<b>Duration of use of HC</b>				
<6 months	77 (62.1)	47 (37.9)	1.00	
6 to 11 months	22 (53.7)	19 (45.2)	0.86 (0.63 – 1.19)	0.366
12 or more months	144 (65.8)	75 (33.6)	1.06 (0.90 – 1.25)	0.504

### Factors associated with dyslipidemias

The variables that were found to be significantly associated with dyslipidemias were BMI (PR=1.33, 95% CI: 1.15 – 1.54, p<0.001) and ART use (PR= 1.21, 95% CI: 1.03 – 1.42, p=0.020). These variables were further assessed for interaction between each other and for confounding with other independent variables; however there was no interaction and the association between dyslipidemias and these variables was not confounded by any other independent variables. Therefore, BMI and ART use were the only independent factors associated with dyslipidemias (Table 3).

**Table 3:** Multivariate analysis of the factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Prevalence Ratio	95% Confidence Interval	P-value
<b>Body Mass Index</b>			
≤25	1.00		
>25	1.33	1.15 – 1.54	<0.001
<b>ART Use</b>			

No	1.00		
Yes	1.21	1.03 – 1.42	0.020

## DISCUSSION

Dyslipidemias were found to be present in more than half of the participants. This high prevalence of dyslipidemias could be an overestimate in the general population because of the differences in these populations; the population in this study had a higher prevalence of ART users (20.3%) than what is reported in the general population (less than 5%),[12] and since ART use is associated with dyslipidemias, the high prevalence could have been as a result of the high percentage on ART. The presence of dyslipidemias in hormonal contraceptive users has been reported by several other studies which found significant changes in the lipid profile levels of hormonal contraceptive users.[7, 15, 17, 18] These changes in the lipid profile levels can be attributed to the lipogenic effect of estrogen in which liver lipogenesis is increased that results in elevated levels of Triglycerides and LDL levels [19]. Furthermore, the progestin component of hormonal contraceptives increases hepatic lipase enzyme activity which increases the removal of HDL hence decreasing the serum HDL levels.[20] These results are however contradicted by a study in China by Wei and his colleagues in 2011 which found no significant association between oral contraceptive use and the risk of dyslipidemias.[10] Wei's study used the same classification of dyslipidemias with the current study (as the presence of one or more abnormal serum lipid profile level), so the difference could have arisen from the fact that Wei's study used a case control design while the current study used a cross sectional design.

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3 The factors found to be significantly associated with dyslipidemias in women using hormonal  
4 contraceptives were BMI and ART use. Participants who had a BMI greater than 25 were  
5 33% more likely to have dyslipidemias compared to those who had a BMI of 25 or less. This  
6 is in line with the findings from a systematic review conducted by Halperin and his  
7 colleagues in 2011 which reported that differences in average BMI of women in the  
8 individual cohorts explained a portion of the heterogeneity found in HDL-C levels.[8] These  
9 changes can be attributed to the fact that BMI can independently affect lipid profile levels as  
10 reported by several studies which observed a significant association between high BMI and  
11 the occurrence of dyslipidemias.[21, 22] The study by Shamai and his colleagues found a  
12 significant association between BMI and both Triglyceride and HDL levels, which was  
13 explained by insulin resistance.[22]

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ART use was the other factor associated with dyslipidemias in women using hormonal  
contraceptives. Women who were using anti-retroviral therapy (ART) were 21% more likely  
to have dyslipidemias than those who were not. These findings should however be treated  
with caution because of the small numbers who were on anti-retroviral therapy in this study.  
This is one of the first studies to report on dyslipidemias in ART users on hormonal  
contraceptives; therefore there are no comparative study findings to use. These changes in  
lipid profile levels can be attributed to the fact that different ART regimens have been  
reported to independently alter lipid profile levels hence aggravating the presence of  
dyslipidemias. A study by Bekolo and his colleagues in 2014 demonstrated a high prevalence  
of dyslipidemias in HIV patients on first line anti-retroviral therapy in Cameroon.[13] This  
was attributed to the fact that some ART regimens exert distinct alterations in lipid  
metabolism hence bringing about dyslipidemias.[14]

Some of the strengths of this study are: This is one of the first studies assessing dyslipidemias  
in women using hormonal contraceptives to be carried out in Uganda and this contributes to

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3 further understanding and possibly better management of dyslipidemias in women using  
4 hormonal contraceptives. In addition, standardised approaches were used when carrying out  
5 this study and this permits the study to be replicated in different areas or over time with an  
6 assurance that the results produced will have comparable findings.  
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11 We acknowledge the following limitations. The findings of this study may not be  
12 generalisable to all hormonal contraceptive users because the sample is not representative  
13 enough and also because the sampling procedure was non-probability which does not allow  
14 equal opportunity to all women to participate. This study was only a cross sectional study so  
15 a causal relationship cannot be ascertained between hormonal contraceptive use and  
16 dyslipidemias. Since questionnaires were used for data collection, some of the self-reported  
17 information may have been inaccurate or incomplete hence affecting some of the results.  
18 Finally, information on the physical activity and diet of the study participants was not  
19 collected which is deemed important for this study since these variables play a significant  
20 role in changing lipid profile levels.  
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33 In conclusion, more than half of the women using hormonal contraceptives have  
34 dyslipidemias and are thus at an increased risk of acquiring cardiovascular diseases.  
35 Hormonal contraceptive users who had a BMI greater than 25 and / or were on anti-retroviral  
36 therapy were more likely to have dyslipidemias and this in the long run increases their risk  
37 for cardiovascular disease. We therefore recommend the Uganda Ministry of Health to  
38 formulate policy to better manage women using hormonal contraceptives. The policy should  
39 include checking lipid profile levels prior to initiation of hormonal contraceptive use and also  
40 continued assessment of lipid profiles at regular intervals while using these contraceptives.  
41 The policy should in particular target the high risk group that includes women whose BMIs  
42 are greater than 25 and / or are on ART. We also recommend that future research is done to  
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3 replicate the study in different populations and also explore whether the relationship between  
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5 dyslipidemias and hormonal contraceptive use is causal.  
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9  
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11  
12 advisers.  
13

14 **Author contribution:**

15  
16 **Ritah Bakesiima** conceptualised the study, designed it, planned the analysis, did the result  
17  
18 interpretation and wrote the manuscript. She is the guarantor and responsible investigator of  
19  
20 the study. **Pauline B Kibwika** planned and supervised the study, interpreted results, and  
21  
22 reviewed the manuscript. **James Tumwine** planned the study, contributed in acquisition of  
23  
24 funds, interpreted results and revised the manuscript. **Joan N Kalyango** planned and  
25  
26 supervised the study and analysis, interpreted results, and revised the manuscript. **Gloria**  
27  
28 **Nabaasa** planned the study, contributed in analysis and reviewed the manuscript. **Irene**  
29  
30 **Najjingo** planned the study, contributed in analysis and reviewed the manuscript. **Grace S**  
31  
32 **Nabaggala** planned the study, contributed in analysis and reviewed the manuscript. **Francis**  
33  
34 **Olweny** planned the study, contributed in analysis and reviewed the manuscript. **Charles**  
35  
36 **Karamagi** conceptualised, planned and supervised the study, interpreted results and reviewed  
37  
38 the manuscript.  
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47

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51 **Competing interests:** The authors declare no competing interests.  
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**Transparency declaration:** *The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.*

**Data sharing:** All available data can be obtained by contacting the corresponding author.

## REFERENCES

1. UNFPA, *Annual Report* (<http://www.unfpa.org/annual-report-2015>). 2015.
2. UDHS, *Millennium Development Goal Indicators* (<http://www.ubos.org/onlinefiles/uploads/ubos/UDHS/UDHS2011.pdf>). 2011.
3. Sabatini, R., R. Cagiano, and T. Rabe, *Adverse Effects of Hormonal Contraception*. J. Reproduktionsmed. Endokrinol 2011. **8**(1): p. 130-156.
4. Gaspard, U., et al., *A randomized study on the influence of oral contraceptives containing ethinylestradiol combined with drospirenone or desogestrel on lipid and lipoprotein metabolism over a period of 13 cycles*. Contraception, 2004. **69**(4): p. 271-8.
5. Schueller, P., et al., *Effects of synthetic progestagens on autonomic tone, neurohormones and C-reactive protein levels in young healthy females in reproductive age*. Int J Cardiol, 2006. **111**(1).
6. Abdel-Barry, J.A., et al., *Lipoprotein changes in women taking low-dose combined oral contraceptive pills: a cross-sectional study in Basra, Iraq*. EMHJ, 2011. **17**(9).
7. Berenson, A., Rahman Mahbubur, and W. Gregg, *Effect of injectable and oral contraceptives on serum lipids*. Obstetrics and gynecology, 2009. **114**(4): p. 786-794.

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8. Halperin, I.J., et al., *The association between the combined oral contraceptive pill and insulin resistance, dysglycemia and dyslipidemia in women with polycystic ovary syndrome: a systematic review and meta-analysis of observational studies*. Hum Reprod, 2011. **26**(1): p. 191-201.
9. Okeke, U., et al., *Comparative Effects of Injectable and Oral Hormonal Contraceptives on Lipid Profile*. European Journal of Medicine, 2011. **2**(1).
10. Wei, W., et al., *Dyslipidaemia, combined oral contraceptives use and their interaction on the risk of hypertension in Chinese women*. Journal of Human Hypertension 2011. **25**: p. 364–371.
11. UBOS, *Uganda demographic and health survey* (<https://dhsprogram.com/pubs/pdf/FR264/FR264.pdf>). 2011.
12. USAID, *HIV Care and Treatment* (<http://sustainuganda.org/content/hiv-care-and-treatment>). 2017.
13. Bekolo, C.E., et al., *The lipid profile of HIV-infected patients receiving antiretroviral therapy in a rural Cameroonian population*. BMC Public Health, 2014. **14**(1): p. 236.
14. Souza, S.J., et al., *Lipid profile of HIV-infected patients in relation to antiretroviral therapy: a review*. Rev Assoc Med Bras (1992), 2013. **59**(2): p. 186-98.
15. Asare, G.A., et al., *Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease in a Ghanaian community*. International Journal of Women's Health, 2014. **6**: p. 597-603.
16. NCEP, *Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)*. Jama, 2001. **285**(19): p. 2486-97.
17. Sitruk-Ware, R., Menard J, and R. M, *Comparison of the impact of vaginal and oral administration of combined hormonal contraceptives on hepatic proteins sensitive to estrogen*. 2007. **75**: p. 430–7.
18. Stocco, B., Fumagalli HF, , et al., *The Effect of Different Contraceptive Drugs on the Lipid Profile of Brazilian Women*. Pharmaceut Anal Acta, 2013. **4**(1).
19. Faryal, U.R., S.: Hajra B, *Lipid profile in females of reproductive age group using combined oral contraceptive pills* Gomal J Med Sci, 2012. **10**: p. 233-6.
20. Yesmin, F., et al., *Lipid Profile in Oral Contraceptives User Women*. Dinajpur Med Col J 2013. **6**(1): p. 54-57.
21. Jayaswal, A.A., *Relation of Body Mass Index with Lipid Profile and Blood Pressure in Healthy Females of Lower Socioeconomic Group, In Kosi Region, Bihar*. Journal of Dental and Medical Sciences 2013. **10**(1): p. 19-21.
22. Shamai, L., et al., *Association of body mass index and lipid profiles: evaluation of a broad spectrum of body mass index patients including the morbidly obese*. Obes Surg, 2011. **21**(1): p. 42-7.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Reported on Page No.
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 - 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 - 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 - 6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 - 6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	-
		(d) If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	-
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7 - 8 and Table 1
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	9 - 10 and

Table 2

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(b) Report category boundaries when continuous variables were categorized	8 – 9, Table 1 and 2
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	2 and 13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11 – 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Dyslipidemias in women using hormonal contraceptives: a cross sectional study in Mulago Hospital Family Planning Clinic, Kampala, Uganda

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Complete List of Authors:	Bakesiima, Ritah; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Byakika-Kibwika, Pauline; Makerere University College of Health Sciences, Department of Internal Medicine Tumwine, James; Makerere University College of Health Sciences, Department of Pediatrics and Child Health Kalyango, Joan; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Nabaasa, Gloria; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Najjingo, Irene; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Nabaggala, Grace; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Olweny, Francis; Makerere University, College of Health Sciences, Clinical Epidemiology Unit Karamagi, Charles; Makerere University College of Health Sciences, Department of Pediatrics and Child Health
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3 **Dyslipidemias in women using hormonal contraceptives: a cross sectional**  
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5 **study in Mulago Hospital Family Planning Clinic, Kampala, Uganda**  
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10 Ritah Bakesiima<sup>1</sup>, Pauline Byakika-Kibwika<sup>2</sup>, James Tumwine<sup>3</sup>, Joan N Kalyango<sup>1</sup>, Gloria  
11 Nabaasa<sup>1</sup>, Irene Najjingo<sup>1</sup>, Grace S Nabaggala<sup>1</sup>, Francis Olweny<sup>1</sup>, Charles Karamagi<sup>3</sup>  
12  
13

14  
15  
16 <sup>1</sup>Clinical Epidemiology Unit, School of Medicine, College of Health Sciences, Makerere  
17 University, Kampala, Uganda  
18

19  
20 <sup>2</sup>Department of Internal Medicine, School of Medicine, College of Health Sciences, Makerere  
21 University, Kampala, Uganda  
22

23  
24 <sup>3</sup>Department of Paediatrics and Child Health, School of Medicine, College of Health  
25 Sciences, Makerere University, Kampala, Uganda  
26  
27  
28

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30  
31 Corresponding author: Ritah Bakesiima  
32

33 (E-mail: [esmie.ritah@gmail.com](mailto:esmie.ritah@gmail.com))  
34

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36 +256772029182, +256706807057  
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**ABSTRACT**

**Objective:** To determine the prevalence and factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic, Kampala, Uganda.

**Design:** Cross sectional study

**Setting:** Mulago Hospital, Kampala, Uganda

**Participants:** Three hundred and eighty four consenting women, aged 18 to 49 years, who had used hormonal contraceptives for at least three months prior to the study.

**Study outcome:** Dyslipidemias (defined as derangements in lipid profile levels which included total cholesterol  $\geq 200$  mg/dL, high-density lipoprotein  $< 40$  mg/dL, triglyceride  $> 150$  mg/dL, or low-density lipoprotein  $\geq 160$  mg/dL) for which the prevalence and associated factors were obtained.

**Results:** The prevalence of dyslipidemias was 63.3% (95% CI: 58.4 – 68.1). Body Mass Index (BMI) (PR=1.33, 95% CI: 1.15-1.54,  $p < 0.001$ ) and use of anti-retroviral therapy (ART) (PR=1.21, 95% CI: 1.03-1.42,  $p = 0.020$ ) were the factors significantly associated with dyslipidemias.

**Conclusion:** Dyslipidemias were present in more than half the participants and this puts them at risk for cardiovascular diseases. The high risk groups were women with a BMI greater than  $25 \text{ Kg/m}^2$  and those who were on ART. Therefore, lipid profiles should be assessed in women using hormonal contraceptives in order to manage them better.

**Keywords:** Hormonal Contraceptives, Contraception, Dyslipidemias, Lipid profile

### Strengths and limitations of the study

- i) This is one of the first studies in Uganda to assess dyslipidemias in women using hormonal contraceptives, hence providing baseline information.
- ii) Standard approaches were used to carry out the study to ensure repeatability and reproducibility.
- iii) Consecutive non-probability sampling was used so the results may not be generalisable to all hormonal contraceptive users.
- iv) Since this was a cross-sectional study, a causal relationship between hormonal contraceptive use and dyslipidemias could not be ascertained.
- v) The results may have been subject to information bias since questionnaires were used to obtain information on some variables based on recall.

### INTRODUCTION

Globally, the use of contraception has risen slightly, from 54.7% in 1990 to 64% in 2015. [1] In Uganda particularly, the Contraceptive Prevalence Rate (CPR) is currently 27.2% with hormonal contraceptives (HCs) accounting for 77.9% of the total contraceptive use.[1] Among the HCs used in Uganda, injectables are the commonest (72.8%), followed by oral contraceptives (14.3%), and implants (12.9%).[2]

Several researchers have reported the complications and side-effects associated with the use of hormonal contraceptives.[3-5] The side effects include nausea and vomiting, headaches, dizziness, breast tenderness and enlargement, irregular bleeding or bleeding between periods, and weight gain. The adverse effects include metabolism impairment, cardiovascular complications, and an increased risk of cancer and liver problems.[3] It has been suggested that some of these complications are a consequence of dyslipidemias, a potential metabolic impairment effect of long term use of some hormonal contraceptives.[5] Furthermore, a study

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3 by Schueller and colleagues suggested that dyslipidemias could also arise from the hormones  
4 increasing apolipoprotein B-100 synthesis, which subsequently increases triglyceride and  
5 LDL levels.[4]  
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9 Several factors predispose hormonal contraceptive users to dyslipidemias. The factors include  
10 age, race, lifestyle and diseases such as hypertension and diabetes mellitus. Medications  
11 especially ART and steroids also contribute.[5-9] Many of these factors are common in  
12 Uganda. For example, 16% of the women in Uganda were found to be obese.[10] Obesity is  
13 associated with alterations in lipid profile levels. In the presence of hormonal contraceptive  
14 use, obesity makes the risk of dyslipidemias worse.[6, 7] In addition, 79% of all HIV infected  
15 women of reproductive age in Uganda are on anti-retroviral therapy (ART).[11] Some anti-  
16 retroviral drugs alter lipid profile levels hence causing dyslipidemias.[12, 13]  
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18 Poorly managed dyslipidemias can result into cardiovascular diseases such as venous  
19 thromboembolism, myocardial infarction and stroke.[14] However, lipid profile levels are not  
20 routinely measured in women using hormonal contraceptives in Uganda. Therefore the  
21 objective of this study was to determine the prevalence and factors associated with  
22 dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning  
23 Clinic, Kampala in Uganda.  
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## 45 **METHODS**

### 46 **Study design, setting and population**

47 This was a cross sectional study employing both descriptive and analytical techniques carried  
48 out from Mulago Hospital Family Planning Clinic in Uganda's Capital City, Kampala from  
49 March to April, 2017. This clinic receives approximately 320 patients monthly, 215 of whom  
50 are on hormonal contraceptives. Using the consecutive sampling procedure, 384 consenting  
51 women aged 18 to 49 years were enrolled into this study. They had to have used hormonal  
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3 contraceptives for at least three months prior to the study. Women who were unable to  
4 comprehend either English or *Luganda* (the local language used in Central Uganda) or those  
5 physically or mentally unable to adhere to study procedures such as giving of consent and the  
6 interview process, were excluded from the study.  
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12 **Ethical issues:** Permission to carry out the study was obtained from the Makerere University  
13 School of Medicine Research and Ethics Committee, Mulago Hospital Ethics Committee, and  
14 the Uganda National Council of Science and Technology. Written informed consent was  
15 obtained from all participants before enrolment into the study and confidentiality was  
16 maintained.  
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24 **Sample size calculation:** The Kish Leslie formula [15] was used to estimate the sample size  
25 for the prevalence objective. We assumed a prevalence of dyslipidemias of 33.9% among  
26 women on oral contraceptives according to a study by Machado in Brazil [16] and 95%  
27 confidence intervals. This gave a sample size of 345. We also accounted for 10% missing data  
28 in the calculation of the sample size. Hence the final sample size was 380.  
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35 For the factors associated with dyslipidemias, the formula for comparing means in two  
36 proportions [17] was used. We assumed an error of 0.05, power of 80% and 95% confidence  
37 level; and that 33.9% of women using oral contraceptives would develop dyslipidemias  
38 compared to only 16.9% of those using non oral contraceptives. We also assumed that the  
39 oral contraceptive prevalence rate in Uganda is 14.3% [2]. This gave a sample size of 384.  
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#### 47 **Data collection**

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49 A questionnaire was administered to collect basic information on age, parity, highest level of  
50 education, occupation, type of hormonal contraceptive used, duration of use of hormonal  
51 contraceptives, use of anti-retroviral drugs and history of hypertension. Body Mass Index  
52 (BMI) was determined by measuring weight using the Seca® weighing scale and height  
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3 using a Seca® stadiometer. BMI was then computed as Weight (in Kg)/Height (in metres  
4 squared). Blood samples were aseptically collected from participants after a six hour fast and  
5 placed in a red top vacutainer without an anticoagulant for the determination of lipid profile  
6 levels. The samples were allowed to clot for at least three minutes and centrifuged at  
7 2400rev/min for five minutes. The serum obtained was pipetted into Cobas® 6000 caps and  
8 taken for analysis using the Cobas® 6000 chemistry analyzer (Roche Diagnostics, USA).  
9 Fasting blood sugar levels were determined using a Freestyle® glucometer (Abott  
10 Laboratories, Canada) for all the participants six hours after their last meal. A sterile single  
11 use lancet was used to prick the participant's disinfected finger and a small drop of the blood  
12 placed onto the glucometer strip already mounted into the glucometer. The blood sugar level  
13 was read off and recorded in mg/dL.  
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### 27 **Outcome variable**

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29 The outcome variable for this study was dyslipidemias defined as derangements in lipid  
30 profile levels which included a total cholesterol of 200 mg/dL or greater, a high-density  
31 lipoprotein cholesterol of less than 40 mg/dL, triglyceride of greater than 150 mg/dL, or low-  
32 density lipoprotein cholesterol of 160 mg/dL or greater according to the Guidelines for the  
33 Diagnosis and Management of Dyslipidemias for Adults.[18] A participant was said to have  
34 dyslipidemias if they had any of the lipid profile parameters in ranges stated above. The  
35 presence of dyslipidemias was coded as “1” and its absence as “0”.  
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### 45 **Statistical analysis**

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47 Data were analysed using STATA version 13.0 (StataCorp. 2013. *Stata Statistical Software:*  
48 *Release 13*. College Station, TX: StataCorp LP) in which all continuous variables were  
49 summarised as medians and ranges while the categorical variables were summarised as  
50 percentages and proportions. The prevalence of dyslipidemias was calculated as the  
51 percentage of women with dyslipidemias over the total number of women in the study. The  
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3 modified Poisson regression model was used to analyse the factors associated with  
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5 dyslipidemias in women using hormonal contraceptives. In the multivariate analysis,  
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7 variables which were significantly associated with dyslipidemias ( $p < 0.05$ ) were used to form  
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9 two-way product terms that were used in the assessment of interaction using the chunk test.  
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11 Where necessary, confounding was assessed for. Confounders were retained only if they  
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13 changed the estimates by greater than or equal to 10%. Confidence intervals were presented  
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15 at 95% level of significance along with the p-values. Statistical significance was considered  
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17 at a p-value of less than or equal to 0.05.  
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### 20 21 **Patient and public involvement**

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23 Due to patients' experiences and complaints raised about excessive weight gain while on  
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25 hormonal contraceptives, we felt the need to determine whether long term use of hormonal  
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27 contraceptives (more than three months) has an effect on lipid profile levels. Hence, patient  
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29 experiences informed our research questions and study outcomes.  
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32 Patients were involved in the design of the study through their contribution to the refining of  
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34 the data collection tool. This was mainly during pre-testing or piloting of the questionnaires.  
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36 Results were disseminated to study participants through the use of text messages and fliers.  
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38 The fliers, printed both in English and *Luganda* were issued out at the family planning clinic.  
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## 43 **RESULTS**

### 44 45 **Participants' characteristics**

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47 The median age of the 384 participants was 28 years (IQR: 18 – 49). An estimated 59.1%  
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49 (227/384) of the participants had attained only up to secondary education, 74.2% (285/384)  
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51 had at least two or more children and 39.6% (152/384) were self-employed. Only 11 (2.9%)  
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53 had high fasting blood sugar levels ( $\geq 120$  mg/dl), 14 (3.7%) had a history of hypertension,  
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55 140 (36.5%) had a BMI  $> 25$  and 78 (20.3%) were on anti-retroviral therapy (ART). Most of  
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the participants were using Progestin-Only Injectables - 185 (48.2%) and 219 (57.0%) had used hormonal contraceptives for over a year (Table 1).

**Table 1:** Social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Number (N=384)	Percentage (%)
<b>Age</b> (Categorised at the median)		
18 – 28	215	56.0
29 – 49	169	44.0
Median (IQR): 28 (18 – 49)		
<b>Education</b>		
No formal education	14	3.6
Primary	107	27.9
Secondary	227	59.1
Tertiary	36	9.4
<b>Parity</b>		
0 - 1	99	25.8
Two or more	285	74.2
<b>Fasting Blood Sugar</b>		
Normal (<120 mg/dl)	373	97.1
High (≥120 mg/dl)	11	2.9
<b>History of Hypertension</b>		
No	370	96.3
Yes	14	3.7
<b>Body Mass Index (BMI)</b>		
≤25	244	63.5
>25	140	36.5
<b>ART Use</b>		
No	306	79.7
Yes	78	20.3
<b>Hormonal Contraceptive Used</b>		
Progestin Only Pill (POP)	5	1.3
Combined Oral Pill (COP)	38	9.9
Progestin Only Injectable (POI)	185	48.2
Combined Injectable Contraceptive (CIC)	8	2.1
Implant (1 rod)	124	32.3
Implant (2 rods)	24	6.2
<b>Duration of use of HC</b>		
<6 months	124	32.3
6 to 11 months	41	10.7
12 or more months	219	57.0

## Prevalence of dyslipidemias

The prevalence of dyslipidemias amongst the 384 participants was 63.3% (95% CI: 58.4 – 68.1). Dyslipidemias were higher in women aged above 28 years (68.0%) compared to those who were younger. The prevalence of dyslipidemias was also higher in participants who had attained up to tertiary education (75%) than those who had acquired lower education. Furthermore, participants who had high fasting blood sugar levels ( $\geq 120$  mg/dl) had more dyslipidemias (81.8%) than those who had normal blood sugar levels (Table 2).

**Table 2:** Prevalence of dyslipidemias according to social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Dyslipidemias Present No. (%)	No Dyslipidemias No. (%)	Prevalence Ratio (95% CI)	P-Value
<b>Overall prevalence of dyslipidemias</b>	243 (63.3)	141 (36.7)	58.4 – 68.1	
<b>Age</b> (Categorised at the median)				
18 – 28	128 (59.5)	87 (40.5)	1.00	
29 – 49	115 (68.0)	54 (32.0)	1.14(0.98-1.32)	<b>0.083</b>
Median = 28 (18 – 49)				
<b>Education</b>				
No formal education	6 (42.9)	8 (57.1)	0.68 (0.37 – 1.25)	<b>0.210</b>
Primary	66 (61.7)	41 (38.3)	0.97 (0.81 – 1.16)	<b>0.759</b>
Secondary	144 (63.4)	83 (36.6)	1.00	
Tertiary	27 (75.0)	9 (25.0)	1.18 (0.96 – 1.46)	<b>0.124</b>
<b>Parity</b>				
0 - 1	59 (59.6)	40 (40.4)	1.00	
$\geq 2$	184 (64.6)	101 (35.4)	1.08 (0.90 – 1.30)	0.394
<b>Fasting Blood Sugar</b>				
Normal	234 (62.7)	139 (37.3)	1.00	
High	9 (81.8)	2 (18.2)	1.30 (0.98 – 1.74)	<b>0.072</b>
<b>History of Hypertension</b>				
No	235 (63.5)	135 (36.5)	1.00	
Yes	8 (57.1)	6 (42.9)	0.90 (0.57 – 1.43)	0.653
<b>Body Mass Index</b>				
$\leq 25$	138 (56.6)	106 (43.4)	1.00	

>25	105 (75.0)	35 (25.0)	1.33 (1.15 – 1.53)	<b>&lt;0.001</b>
<b>ART Use</b>				
No	186 (60.8)	120 (39.2)	1.00	
Yes	57 (73.1)	21 (26.9)	1.20 (1.02 – 1.41)	<b>0.026</b>
<b>Hormonal Contraceptive Used</b>				
Oral Contraceptives	22 (51.2)	21 (48.8)	1.77 (0.57 – 1.05)	<b>0.100</b>
Injectables	128 (66.3)	65 (33.7)	1.00	
Implants	93 (63.8)	55 (35.2)	0.95 (0.81 – 1.11)	<b>0.508</b>
<b>Duration of use of HC</b>				
<6 months	77 (62.1)	47 (37.9)	1.00	
6 to 11 months	22 (53.7)	19 (45.2)	0.86 (0.63 – 1.19)	0.366
12 or more months	144 (65.8)	75 (33.6)	1.06 (0.90 – 1.25)	0.504

### Factors associated with dyslipidemias

Variables significantly associated with dyslipidemias included BMI greater than 25kg/m<sup>2</sup> (PR=1.33, 95% CI: 1.15 – 1.54, p<0.001) and ART use (PR= 1.21, 95% CI: 1.03 – 1.42, p=0.020). These variables were further assessed for interaction between each other and for confounding with other independent variables. However there was no interaction and the association between dyslipidemias and these variables was not confounded by any other independent variables. Therefore, BMI and ART use were the only independent factors associated with dyslipidemias (Table 3).

**Table 3:** Multivariate analysis of the factors associated with dyslipidemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March to April, 2017

Variable	Prevalence Ratio	95% Confidence Interval	P-value
<b>Body Mass Index</b>			
≤25	1.00		
>25	1.33	1.15 – 1.54	<0.001
<b>ART Use</b>			
No	1.00		
Yes	1.21	1.03 – 1.42	0.020

## DISCUSSION

Dyslipidemias were present in more than half the participants. This high prevalence of dyslipidemias could be an over estimate in the general population because of the differences in these populations. This study had a higher prevalence of anti-retroviral therapy (ART) users (20.3%) than what is reported in the general population (less than 5%).<sup>[11]</sup> Since ART use is associated with dyslipidemias, the high prevalence obtained could have been as a result of the high percentage on ART.

The presence of dyslipidemias in hormonal contraceptive users has been reported by several other studies which found significant changes in the lipid profile levels of hormonal contraceptive users.<sup>[5, 6, 14, 19]</sup> These changes in the lipid profile levels can be attributed to the lipogenic effect of estrogen in which liver lipogenesis is increased and results in elevated levels of Triglycerides and LDL levels <sup>[20]</sup>. Furthermore, the progestin component of hormonal contraceptives increases hepatic lipase enzyme activity which increases the removal of HDL hence decreasing the serum HDL levels.<sup>[21]</sup>

The factors significantly associated with dyslipidemias in women using hormonal contraceptives were BMI and ART use. Participants who had a BMI greater than 25kg/m<sup>2</sup> were 33% more likely to have dyslipidemias compared to those who had a BMI of 25kg/m<sup>2</sup> or less. This is in line with the findings from a systematic review by Halperin and colleagues in 2011. Halperin's study reported that differences in average BMI of women in the individual cohorts explained a portion of the heterogeneity found in HDL-C levels.<sup>[7]</sup> These changes can be attributed to BMI independently affecting lipid profile levels as reported by studies which observed a significant association between high BMI and the occurrence of dyslipidemias.<sup>[22, 23]</sup> A study by Shamai and colleagues reported a significant association

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3 between BMI and both Triglyceride and HDL levels, which was attributed insulin  
4 resistance.[23]

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7 ART use was the other factor associated with dyslipidemias in women using hormonal  
8 contraceptives. Women who were using anti-retroviral therapy (ART) were 21% more likely  
9 to have dyslipidemias than those who were not. This is one of the first studies to report on  
10 dyslipidemias in ART users on hormonal contraceptives; therefore there are no studies with  
11 which to compare our results. These changes in lipid profile levels can be attributed to some  
12 ART regimens exerting distinct alterations in lipid metabolism hence bringing about  
13 dyslipidemias.[13] A study by Bekolo and colleagues in 2014 demonstrated a high  
14 prevalence of dyslipidemias in HIV patients on first line anti-retroviral therapy in  
15 Cameroon.[12]

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18 Some of the strengths of this study are: This is one of the first studies assessing dyslipidemias  
19 in women using hormonal contraceptives to be carried out in Uganda. This contributes to  
20 further understanding and possibly, better management of dyslipidemias in women using  
21 hormonal contraceptives. In addition, standardised approaches were used when carrying out  
22 this study and this permits the study to be replicated in different areas or over time with an  
23 assurance that the results produced will have comparable findings.

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26 We acknowledge the following limitations. The findings of this study may not be  
27 generalisable to all hormonal contraceptive users because the sample is not representative  
28 enough. The sampling procedure used was non-probability and this does not allow equal  
29 opportunity to all women to participate. As this was a cross sectional study, a causal  
30 relationship cannot be established between hormonal contraceptive use and dyslipidemias.  
31 Since questionnaires were used for data collection, some of the self-reported information may  
32 have been inaccurate hence affecting some of the results. Finally, information on the physical  
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3 activity and diet of the study participants was not collected. This information is important  
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5 since these variables play a significant role in changing lipid profile levels.  
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7 In conclusion, more than half the women using hormonal contraceptives had dyslipidemias  
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9 and are thus at an increased risk of acquiring cardiovascular diseases. Hormonal  
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11 contraceptive users who had a BMI greater than 25kg/m<sup>2</sup> and / or were on anti-retroviral  
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13 therapy were more likely to have dyslipidemias and this in the long run increases their risk  
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15 for cardiovascular disease.  
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17 We therefore recommend the Uganda Ministry of Health to formulate policy to better manage  
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19 women using hormonal contraceptives. The policy should include checking lipid profile  
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21 levels prior to initiation of hormonal contraceptive use and also continued assessment at  
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23 regular intervals while using contraceptives. The policy should in particular target the high  
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25 risk group that includes women whose BMI is greater than 25kg/m<sup>2</sup> and / or are on ART.  
26  
27 Further studies are urgently needed to explore whether the relationship between  
28  
29 dyslipidemias and hormonal contraceptive use is causal.  
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43 **Author contribution:**

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45 **Ritah Bakesiima** conceptualised the study, designed it, planned the analysis, did the result  
46  
47 interpretation and wrote the manuscript. She is the guarantor and responsible investigator of  
48  
49 the study. **Pauline B Kibwika** planned and supervised the study, interpreted results, and  
50  
51 reviewed the manuscript. **James Tumwine** planned the study, contributed in acquisition of  
52  
53 funds, interpreted results and revised the manuscript. **Joan N Kalyango** planned and  
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55 supervised the study and analysis and interpreted results. **Gloria Nabaasa** planned the study  
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3 and contributed in analysis. **Irene Najjingo** planned the study and contributed in analysis.  
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5 **Grace S Nabaggala** planned the study and contributed in analysis. **Francis Olweny** planned  
6  
7 the study and contributed in analysis. **Charles Karamagi** conceptualised, planned and  
8  
9 supervised the study, interpreted results and reviewed the manuscript. All authors have read  
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11 the final manuscript.  
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32 National Referral Hospital.  
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51 *the study have been omitted; and that any discrepancies from the study as planned have been*  
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53 *explained.*  
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**Data sharing:** All available data can be obtained by contacting the corresponding author.

## REFERENCES

1. UNFPA, *Annual Report* (<http://www.unfpa.org/annual-report-2015>). 2015.
2. UDHS, *Millennium Development Goal Indicators* (<http://www.ubos.org/onlinefiles/uploads/ubos/UDHS/UDHS2011.pdf>). 2011.
3. Sabatini, R., R. Cagiano, and T. Rabe, *Adverse Effects of Hormonal Contraception*. J. Reproduktionsmed. Endokrinol 2011. **8**(1): p. 130-156.
4. Schueller, P., et al., *Effects of synthetic progestagens on autonomic tone, neurohormones and C-reactive protein levels in young healthy females in reproductive age*. Int J Cardiol, 2006. **111**(1).
5. Stocco, B., Fumagalli HF, , et al., *The Effect of Different Contraceptive Drugs on the Lipid Profile of Brazilian Women*. Pharmaceut Anal Acta, 2013. **4**(1).
6. Berenson, A., Rahman Mahbubur, and W. Gregg, *Effect of injectable and oral contraceptives on serum lipids*. Obstetrics and gynecology, 2009. **114**(4): p. 786-794.
7. Halperin, I.J., et al., *The association between the combined oral contraceptive pill and insulin resistance, dysglycemia and dyslipidemia in women with polycystic ovary syndrome: a systematic review and meta-analysis of observational studies*. Hum Reprod, 2011. **26**(1): p. 191-201.
8. Okeke, U., et al., *Comparative Effects of Injectable and Oral Hormonal Contraceptives on Lipid Profile*. European Journal of Medicine, 2011. **2**(1).
9. Wei, W., et al., *Dyslipidaemia, combined oral contraceptives use and their interaction on the risk of hypertension in Chinese women*. Journal of Human Hypertension 2011. **25**: p. 364–371.
10. UBOS, *Uganda demographic and health survey* (<https://dhsprogram.com/pubs/pdf/FR264/FR264.pdf>). 2011.
11. UNAIDS, *UNAIDS Country factsheets Uganda 2017*. 2017.
12. Bekolo, C.E., et al., *The lipid profile of HIV-infected patients receiving antiretroviral therapy in a rural Cameroonian population*. BMC Public Health, 2014. **14**(1): p. 236.
13. Souza, S.J., et al., *Lipid profile of HIV-infected patients in relation to antiretroviral therapy: a review*. Rev Assoc Med Bras (1992), 2013. **59**(2): p. 186-98.
14. Asare, G.A., et al., *Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease in a Ghanaian community*. International Journal of Women's Health, 2014. **6**: p. 597-603.
15. Kish, L., *Survey Sampling*. New York: John Wiley and Sons, Inc. 1965: p. 78-94.
16. Machado, R.B., et al., *Is lipid profile determination necessary in women wishing to use oral contraceptives?* Contraception, 2013. **87**(6): p. 801-5.
17. Hulley, S.B., et al., *Designing Clinical Research 4th Edition*. 4th ed. 2013.
18. Stein, J., et al., *Guidelines for the Diagnosis and Management of Dyslipidemias for Adults ≥ 18 Years Old*. 2008.
19. Sitruk-Ware, R., Menard J, and R. M, *Comparison of the impact of vaginal and oral administration of combined hormonal contraceptives on hepatic proteins sensitive to estrogen*. 2007. **75**: p. 430–7.
20. Faryal, U.R., S.: Hajra B, *Lipid profile in females of reproductive age group using combined oral contraceptive pills* Gomol J Med Sci, 2012. **10**: p. 233-6.
21. Yesmin, F., et al., *Lipid Profile in Oral Contraceptives User Women*. Dinajpur Med Col J 2013. **6**(1): p. 54-57.

- 1  
2  
3 22. Jayaswal, A.A., *Relation of Body Mass Index with Lipid Profile and Blood Pressure in Healthy*  
4 *Females of Lower Socioeconomic Group, In Kosi Region, Bihar.* Journal of Dental and Medical  
5 Sciences 2013. **10**(1): p. 19-21.  
6 23. Shamaï, L., et al., *Association of body mass index and lipid profiles: evaluation of a broad*  
7 *spectrum of body mass index patients including the morbidly obese.* Obes Surg, 2011. **21**(1):  
8 p. 42-7.  
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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Reported on Page No.
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 - 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 - 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	4 - 5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 - 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 - 6
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6 - 7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6 - 7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	-
		(d) If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	-
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7 - 8 and Table 1
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	9 - 10 and

Table 2

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(b) Report category boundaries when continuous variables were categorized	8 – 9, Table 1 and 2
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	2 and 13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11 – 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).