TITLE

Hormonal Contraception and Hemoglobin Levels in Urban Malawi: A Longitudinal Analysis

SHORT RUNNING HEAD

Hormonal Contraception and Hemoglobin Levels

AUTHOR NAMES

Mahesh Karra

David Canning

AUTHOR AFFILIATIONS

MK: Frederick S. Pardee School of Global Studies, Boston University, 152 Bay State Road, Room G04C, Boston, MA 02215

DC: Department of Global Health and Population, Harvard T.H. Chan School of Public Health, 665 Huntington Avenue, SPH I 1211, 12th Floor, Boston, MA 02115

CORRESPONDING AUTHOR

Mahesh Karra

Frederick S. Pardee School of Global Studies

Boston University

152 Bay State Road, Room G04C

Boston, MA 02215

mvkarra@bu.edu

Declarations

Ethics Approval and Consent to Participate

Ethical approval to conduct the study was received from the Harvard University Institutional Review Board (protocol number IRB16-0421) and from the Malawi National Health Sciences Research Committee (protocol number 16/7/1628). Written informed consent to participate in the study was obtained, and only women who consented were recruited into the study.

Availability of Data and Materials

Deidentified data and replication code for this study will be made available on the Harvard DataVerse repository at https://dataverse.harvard.edu.

Funding

The main trial was funded through two grants from the William and Flora Hewlett Foundation (Grants 2014-9952 and 2017-5795). Supplemental funding support for piloting, travel, and fieldwork was provided by the Global Development Policy Center at Boston University, the Harvard Center for Population and Development Studies, the Harvard Center for African Studies, and the Harvard Institute for Quantitative Social Science (IQSS). Support for this study was provided by the Program for Women's Empowerment Research (POWER) at the Global Development Policy Center through a grant from the William and Flora Hewlett Foundation (Grant No. 2020-1162). The study funders had no role in study design, data collection, analysis, interpretation, or writing of the results.

Competing Interests

We declare that no competing interests exist, and all errors are our own.

Author Contributions

MK and DC designed the trial protocol and instruments. MK led the field implementation and monitored the trial implementation. MK and DC contributed to data management and analysis. MK and DC coordinated the project between Malawi and Harvard University. MK wrote the first draft of the manuscript with the contributions of DC. MK and DC contributed toward data analysis, drafting, and revising the paper and have agreed to be accountable for all aspects of the work. All authors have read and approved the final manuscript.

Abstract

Background

Studies have highlighted potential non-contraceptive benefits from women's use of hormonal, reversible contraceptive methods. Given the physiological pathways through which hormonal contraception may interact with menstruation, a growing body of work has documented the extent to which hormonal method use might be associated with increased hemoglobin levels and reductions in the risk of anemia in women. While these findings are promising, the scope for causal inference from these studies is restricted by their cross-sectional design, which limits the extent to which bias from individual-level confounding can be mitigated.

Methods

We assess the relationship between women's use of hormonal contraception and their risk of anemia using three years of annual woman-level panel data on 2143 women from urban Malawi controlling for individual woman fixed effects. We compare our panel results with cross-sectional estimates from the same sample.

Results

We find that hormonal method use is associated with increased levels of hemoglobin in women, though the effects are different for different hormonal methods.. Adoption of an injectable is associated with a 3.7 g/cL increase, and adoption of an implant a 5.7 g/cL increase, in hemoglobin levels. Our estimates are consistent across cross-sectional and panel model specifications, suggesting that existing cross-sectional estimates may be reliable.

Conclusions

Our findings highlight potential health benefits from hormonal contraceptive use that extend beyond pregnancy prevention. These benefits, in turn, have significant implications as to how women are counseled on contraception both within family planning and nutrition programs.

Trial Registration

This trial was registered at the American Economics Association Registry for randomized controlled trials on May 7, 2015 (AEARCTR-0000697) and at the Registry for International Development Impact Evaluations (RIDIE) on May 28, 2015 (RIDIE-STUDY-ID-556784ed86956).

Plain English Summary

The use of hormonal, reversible contraception might have potential non-contraceptive benefits in addition to reducing the risk of pregnancy. There is cross sectional evidence that women using hormonal methods have higher hemoglobin levels, and lower likelihood of anemia, than non-hormonal method users. The cross-sectional association may be due to differences between the types of women who use different contraceptive methods. We use a three wave annual panel data of study the relationship between changes in hormonal contraceptive use and changes in hemoglobin levels using data from urban Malawi. We find that adopting a hormonal method is associated with an increased level of hemoglobin, though different hormonal methods appear to have different effect sizes. Our findings suggest that hormonal contraception may confer additional health benefits beyond their primary function to prevent pregnancy. We highlight the importance for women to be counseled on these benefits so that they are able to make more informed decisions over their contraceptive use and choice of method.

Background

Most methods of contraception were developed with the goal of preventing unintended and mistimed pregnancies in mind. However, a growing body of research has also identified potential non-contraceptive benefits from contraceptive method use, particularly from the use of hormonal, reversible contraceptive methods such as the intrauterine device (IUD), the contraceptive implant, injectable contraception, and the oral contraceptive pill (1,2). Some studies have examined the extent to which the use of oral contraceptives and IUDs may reduce the risk of gynecological cancers, while others have documented the effectiveness of these methods as treatments for a wide range of conditions, including irregular and heavy menstrual bleeding, dysmenorrhea, premenstrual syndrome, and endometriosis, among others (3–6). In addition, a number of studies have explored the role of hormonal contraception in reducing the risk of non- gynecological conditions, such as severe asthma (7) or colorectal cancer (8–10). At the same time, studies have also identified potential risks and side effects associated with hormonal contraceptive use, including thromboembolic events (11), breast cancer (12), and some sexually transmitted infections (13).

Given the physiological pathways through which hormonal contraception may interact with menstrual flow, anovulatory bleeding, and other related conditions, a growing body of work has documented the extent to which hormonal method use might be associated with reductions in the risk of anemia in women. Anemia, which is characterized by low hemoglobin levels in the bloodstream, affects more than 2.2 billion people globally and an estimated 4 in 10 people in low- and middle-income countries (14,15). Anemia is more commonly observed in children and in women of reproductive age; however, while the primary cause of anemia in children is insufficient iron in the diet, anemia in women can also be due to blood loss during menstruation and pregnancy (16,17). Low concentrations of blood-level hemoglobin have been linked to adverse physical and cognitive health outcomes (fatigue, low

energy, poor productivity), and anemia during pregnancy has also been associated with increased risks of maternal mortality and morbidity (18,19).

A number of studies, including several from low- and middle-income countries, have assessed the correlation between hormonal contraceptive use and increased hemoglobin levels, leading to a reduction in women's risk of anemia (20–25). While these findings are promising, the scope for causal inference from these studies is restricted by their cross-sectional design, which limits the extent to which bias from individual-level confounding can effectively be mitigated. In cross-sectional studies, it is difficult to distinguish if a correlation between contraceptive use and hemoglobin levels is due to an effect of the contraceptive, or whether women of a particular type, who tend to use a particular contraceptive method, are more likely to have elevated or depressed hemoglobin levels independently of their use. This can be partially addressed by adding control variables, but it is difficult to ensure that all relevant factors have been accounted for so as to eliminate confounder bias. In addition, we note that some studies have examined the broader categorical effect of hormonal versus non-hormonal contraceptive methods on anemia, while other studies have documented the effect of each specific method separately. The separation of effect size by method may be important because different hormonal methods (oral contraceptives, implants, injectables, and IUDs) use different types of hormones at different concentrations and have different time patterns of hormone release (26,27).

In this study, we assess the relationship between women's use of hormonal contraception and changes to their risk of anemia using panel data on women from urban Malawi. We document the extent to which women's adoption of hormonal contraceptive methods following pregnancy relates to changes to their hemoglobin level. The panel data allows us to control for individual woman fixed effects, capturing all women specific characteristics that are time invariant. More directly, the cross-sectional

approach asks if using a contraceptive method is associated with a higher hemoglobin level, while the fixed effects approach asks if a woman's hemoglobin level changes when she changes to a new contraceptive method. Our longitudinal data structure thus allows us to provide more rigorously identified estimates of these relationships.

An important issue that we examine is to determine whether using the panel data approach with fixed effects changes the results of the analysis relative to the cross-sectional estimates; this comparison would indicate the extent to which the existing body of evidence that is based on cross-sectional data may be reliable. We make this comparison by testing whether models with individual women fixed effects yield different coefficient estimates than models that assume that any individual woman-level effects are random and are therefore uncorrelated with contraceptive use and do not confound the relationship. If we find that the panel data approach with individual fixed effects does not significantly affect coefficient estimates, it will indicate the reliability of the results from studies that use cross-sectional approaches.

Methods

Data

We use three waves of longitudinal data that were collected as part of a randomized controlled trial of a family planning intervention in urban Malawi that was conducted between 2016 and 2019; a more detailed description of the study design and data collection approach is presented elsewhere (28,29). As part of the trial, 2,143 women who were either pregnant or immediately postpartum (within 6 months of their last live birth), between the ages of 18 and 35, and living in Lilongwe, the capital, were recruited in 2016. Following a baseline survey, which was conducted from 2016 to 2017, women were individually randomized to either an intervention arm or control arm. Women assigned to the

intervention arm received a multicomponent package of family planning services over a two-year period. Two annual follow-up surveys were conducted with all women from 2017 to 2018 and from 2018 to 2019, respectively. Our data are measured using a range of validated metrics and instruments. In particular, our baseline and follow-up survey instruments are comprised of modules from the household and women's questionnaires from the Malawi Demographic and Health Survey (DHS) and includes information on fertility, family planning, reproductive health, and maternal health (30).

Key Exposure: Use of Hormonal Contraception

In each survey wave, women are asked to report their contraceptive use, history of contraceptive use or non-use since the last interview, and the type of contraceptive method(s) that they are currently using. We classify a woman to be using hormonal contraception if she reports using either the contraceptive implant (Jadelle), injectable contraception (Depo-Provera), or the oral contraceptive pill at the time of interview. In our study setting, only a nonhormonal IUD brand (specifically, the copper IUD) was available to women at the time when the study was conducted; we therefore assign a woman who reports using an IUD at the time of interview to be using a nonhormonal method.

Key Outcomes: Hemoglobin Levels

For women who were enrolled in the study, anthropometric data that included height, weight, and hemoglobin measures, as an indicator for anemia, were collected in all three survey waves. The study team measured women's hemoglobin levels (in g/cL) using a rapid, on-site blood diagnostic test, the HemoCue 201+ point-of-care system, and followed the standard DHS protocols for the collection and management of blood biomarker data. For our study, we analyze the role of women's contraceptive use, and particularly hormonal contraception, on measured hemoglobin levels at the time of the survey (in g/cL).

Throughout the study, hemoglobin measurement rates among eligible women are low. Two factors drive these low rates. First, this study was conducted in a densely urban environment where women were often not available at home and therefore had to often be interviewed by phone; anthropometric and hemoglobin measurements were therefore not collected for these women. Second, we observe a consistently low rate of consent among women across our surveyed waves, which may, in part, have been driven by religious beliefs and mistrust around the collection and handling of blood.[1] As a result, we were forced to halt all on-site blood testing for anemia, out of concern for the safety of our field research team.

Analysis

Our main empirical models exploit the longitudinal study design. Specifically, we run linear panel models with two-way (woman-level and survey wave-level) fixed effects as follows:

$$Y_{it} = \beta Method_{it} + \boldsymbol{X}_{it}\boldsymbol{\gamma} + \delta_i + \eta_t + \varepsilon_{it}$$

where Y_{it} is the measured hemoglobin level for woman i at survey wave t. $Method_{it}$ is a categorical variable that identifies the type of contraceptive method used (with non-use coded as 0); we also run specifications that classifies a woman's method use as a categorical variable, taking on a value of 2 if the woman reported using a hormonal contraceptive method at survey wave t, 1 if the woman reported using a non-hormonal contraceptive method at t, and 0 otherwise. $\boldsymbol{X}_{it}$ represents a vector of time-varying covariates, including women's work status (working / not working), whether the

[1] The level of mistrust over the collection of blood samples for research was exacerbated in September and October 2017, when at least five people were killed by lynch mobs who accused them of vampirism. News sources reported that mobs searching for accused vampires in communities had been mounting roadblocks, which raised safety and security concerns throughout the country (31). In response to these rumors, the United Nations, international NGOs, and other institutions in Malawi withdrew many staffers from southern districts and temporarily suspended any research-related collection of blood samples from respondents.

women own agricultural land (yes / no), body mass index (BMI) at the time of the survey, educational attainment (none, primary, secondary, or higher), and parity, measured by the total number of children to whom the woman has given birth. To account for unobserved woman-level and temporal variation, we include individual woman-level fixed or random effects (δ_i) as well as survey wave fixed effects (η_t); finally, ε_{it} represents the error term.

To compare our panel estimates with previous cross-sectional approaches, we run a linear ordinary least-squares (OLS) regression specification using cross-sectional data from the third (2018-2019) survey wave as follows:

$$Y_i = \alpha + \beta Method_i + \boldsymbol{Z}_i\boldsymbol{\gamma} + \nu_i$$

where $\boldsymbol{Z}_i$ represents a vector of individual-level covariates that were collected for each woman i in that wave, including women's work status (working / not working), whether the women own agricultural land (yes / no), body mass index (BMI) at the time of the survey, educational attainment (none, primary, secondary, or higher), ever use of contraception (yes / no), age (in years), pregnancy status at the time of the survey (yes / no), and parity, measured by the total number of children to whom the woman has given birth. We note that in the cross-sectional model, the error term ν_i is equivalent to the sum of individual random effect δ_i and the random error term ε_{it} in the panel models.

Comparing Models

The fixed effects model is more general than the random effects approach. With fixed effects, we allow for the unobserved woman-level characteristics δ_i to be correlated with a woman's contraceptive method use $Method_{it}$; specifically, women who use different methods may have different unobserved characteristics. In contrast, the random effects model is more restrictive in that it assumes that a

woman's contraceptive use is uncorrelated with any unobserved characteristics for the woman. While the random effects model is less general, it is a more efficiently estimated model if the assumption that the unobserved characteristics are random is indeed true. This is due to the fact that the fixed effect model requires the estimation of each woman-level fixed effect, which reduces the model's degrees of freedom and leads to wider confidence intervals for the estimated parameters of interest.

We test if the assumptions of the random effect model hold relative to the fixed effects model by calculating the Wu-Hausman F-statistic for parameter equality between the parameter estimates of the fixed effects and random effects models (32,33). Rejection of equality using this test is evidence that the random effects parameter estimates are biased and the fixed effect estimates are consistent. In contrast, failure to reject parameter equality indicates that the random effects assumption may be correct and the fixed effects estimates, though also consistent, may be less efficient. In addition to testing for parameter equality overall, we can test each parameter individually for equality across the two models to observe which parameters seem to be biased if the results differ.

Results

Table 1 presents descriptive statistics by survey wave, and Appendix Figure 1 presents a flowchart as to how the analytic sample was obtained after accounting for observations with missing data in our key outcomes and other variables of interest. We observe an increase in measured hemoglobin levels in our sample between the first survey and subsequent waves, which is indicative of postnatal recovery in our sample of pregnant and immediate postpartum women from when they were initially recruited at baseline. Figure 1 presents the rightward shift in the distribution of measured hemoglobin in our sample from baseline (2016) to endline (2018), which provides additional evidence of this recovery

over time. Similarly, anemia prevalence in our sample decreases over time from 57 percent in 2016 (when women were either pregnant or postpartum at recruitment) to 29.1 percent in 2018.

Contraceptive use in our sample increases considerably over the study period, from 21.7 percent in 2016 to 85.8 percent in 2018. Finally, we note that hormonal method use makes up a significant majority (accounting for more than 90 percent) of all contraceptive use by women in our sample in any year.

Table 2 presents estimates from our cross-sectional OLS, fixed effects, and random effects panel regressions, respectively. Across all three specifications, we note a positive association between hormonal contraceptive method use, particularly the injectable and the implant, and hemoglobin levels in women. Our cross-sectional results (column 1) indicate that compared to non-users of contraception (the reference group), injectable and implant use among women in 2018 is associated with a 4.7 g/cL and a 7.3 g/cL increase in hemoglobin levels, respectively. In contrast, our random effects results (column 3) indicate that a change in women's method use from non-use to injectable and implant use (i.e. adoption of the method) between 2016 and 2018 is associated with a 3.7 g/cL and 5.7 g/cL respective increase in their hemoglobin levels. Estimates from our fixed effects model (column 2) show a similar, but smaller positive association between these hormonal methods and hemoglobin in women over our study period. In comparing the coefficients from the random effects and fixed effects models (Table 3), we find significantly larger estimates in the random effects model relative to the fixed effects model for the injectable and the pill. In addition, a formal Wu-Hausman test of parameter equality shows that we fail to reject parameter equality between the two models, indicating that the random effects model, as the more efficient model, would be preferred.

In Table 4, we present estimates from our three models that use a coarser categorical indicator of contraceptive use (non-use, non-hormonal method use, and hormonal method use). Our findings are qualitatively consistent with the estimates that we obtain from the models that examine methods separately. With this said, we note that the estimated association between hormonal method use and hemoglobin levels in the fixed effects model are smaller and insignificant relative to the random effects model, which highlight a 3.9 g/cL associated increase in hemoglobin levels with hormonal method use. Findings from the Wu-Hausman test (Table 5) indicate significant differences in the fixed effects model estimates relative to the random effects model, to the extent that we would reject the null hypothesis of parameter equality in favor of the fixed effects model.

Discussion

We assess the relationship between Malawian women's hormonal contraceptive use and their risk of anemia, measured by hemoglobin levels, using a range of panel and cross-sectional approaches. We find that hormonal method use, particularly implant use and (to a lesser degree) injectable use, is associated with increased levels of hemoglobin in women. These estimates are consistent across model specifications.

Our main method-specific analyses yield two principal findings. First, we note that our results from adding individual woman-level fixed effects in a panel data approach are not significantly different from those that we obtain when using a random effects model. Second, we do not find sufficient evidence to conclude that the cross-sectional association between contraceptive method use and hemoglobin levels is due to unobserved women characteristics; specifically, we note the overlap in the confidence intervals between our cross-sectional OLS estimates and panel models.

In contrast, we do find that compared to the cross-section results, the fixed effects and random effects approaches give significantly different results when we aggregate contraceptive methods into hormonal and non-hormonal method groups. In this case, the estimated coefficient on hormonal methods using the fixed effects approach is smaller and less significant than that the coefficient that we estimate using random effects and cross-section approaches. However, we do not think that this observed difference in estimates is necessarily due to differences in how individual heterogeneity is accounted for in each model, but rather due to variable misspecification in the models in which all hormonal methods are grouped together. This is because the cross-sectional models estimate the associations between the mix of hormonal methods being used and hemoglobin levels, whereas the panel models with fixed (or random) effects estimate the within-woman associations between changes to hormonal method use through either adoption or discontinuation and changes to hemoglobin levels. The patterns in current hormonal method use across women and the patterns in adoption and discontinuation among these methods within each woman may be inherently different, which would likely yield different effect size estimates if different hormonal methods have different effects on hemoglobin.

In this study, we focus on the effect of contraceptive method use on hemoglobin levels rather than on anemia. Anemia is a binary outcome that is based on cut points in the hemoglobin level to delineate levels of severity (34). The analysis of panel data using fixed effects for binary or categorical outcomes can still be carried out using the conditional logit model but is problematic because the fixed effect is not identified for any women who do not change their anemia status; as a result, these women are dropped from the estimation (35). This leaves us with a very small sample size and limited power for examining anemia using the fixed effects approach, and it becomes difficult to draw conclusions from this approach.

Conclusions

Our study reinforces the evidence base that identifies an effect of hormonal contraceptive use on hemoglobin levels using cross-sectional data, and our findings suggest that the cross-sectional results may be reliable. However, we caution that grouping all hormonal methods together, thereby treating them as having a common effect size, may be misleading and may give rise to differences in estimated effect sizes as the composition of individual methods within the method group change. Taken together, our findings highlight potential health benefits from hormonal contraceptive use that extend beyond their primary function to prevent pregnancy. These benefits, in turn, have significant implications as to how women are counseled on contraception both within family planning and nutrition programs. At the very least, awareness of these potential advantages during contraceptive counseling would help women to make more informed reproductive health choices.

List of Abbreviations

DHS: Demographic and Health Survey

IUD: intrauterine device

OLS: ordinary least-squares regression

References

1. Maguire K, Westhoff C. The state of hormonal contraception today: established and emerging noncontraceptive health benefits. American Journal of Obstetrics and Gynecology. 2011 Oct 1;205(4, Supplement):S4–8.
2. Schindler AE. Non-contraceptive use of hormonal contraceptives. Gynecological Endocrinology. 2008 Jan;24(5):235–6.
3. Fraser IS. Non-contraceptive health benefits of intrauterine hormonal systems. Contraception. 2010 Nov 1;82(5):396–403.
4. Fraser IS, Kovacs GT. The efficacy of non-contraceptive uses for hormonal contraceptives. Medical Journal of Australia. 2003 Jun;178(12):621–3.
5. Huber JC, Bentz EK, Ott J, Tempfer CB. Non-contraceptive benefits of oral contraceptives. Expert Opinion on Pharmacotherapy. 2008 Sep 1;9(13):2317–25.
6. Jensen JT. The benefits of reduced menstrual bleeding associated with the use of contraceptive methods. In: Gynecological Forum. 15; 2010.
7. Nwaru BI, Tibble H, Shah SA, Pillinger R, McLean S, Ryan DP, et al. Hormonal contraception and the risk of severe asthma exacerbation: 17-year population-based cohort study. Thorax. 2021 Feb 1;76(2):109–15.
8. Bahamondes L, Valeria Bahamondes M, Shulman LP. Non-contraceptive benefits of hormonal and intrauterine reversible contraceptive methods. Human Reproduction Update. 2015 Sep 1;21(5):640–51.
9. Fernandez E, Vecchia CL, Balducci A, Chatenoud L, Franceschi S, Negri E. Oral contraceptives and colorectal cancer risk: a meta-analysis. Br J Cancer. 2001 Mar;84(5):722–7.
10. Cibula D, Gompel A, Mueck AO, La Vecchia C, Hannaford PC, Skouby SO, et al. Hormonal contraception and risk of cancer. Human Reproduction Update. 2010 Nov 1;16(6):631–50.
11. Shulman LP. The state of hormonal contraception today: benefits and risks of hormonal contraceptives: combined estrogen and progestin contraceptives. American Journal of Obstetrics and Gynecology. 2011 Oct 1;205(4, Supplement):S9–13.
12. Mørch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard Ø. Contemporary Hormonal Contraception and the Risk of Breast Cancer. New England Journal of Medicine. 2017 Dec 7;377(23):2228–39.
13. Baeten JM, Nyange PM, Richardson BA, Lavreys L, Chohan B, Martin HL, et al. Hormonal contraception and risk of sexually transmitted disease acquisition: Results from a prospective study. American Journal of Obstetrics and Gynecology. 2001 Aug 1;185(2):380–5.
14. Lopez A, Cacoub P, Macdougall IC, Peyrin-Biroulet L. Iron deficiency anaemia. The Lancet. 2016 Feb 27;387(10021):907–16.
15. Karami M, Chaleshgar M, Salari N, Akbari H, Mohammadi M. Global Prevalence of Anemia in Pregnant Women: A Comprehensive Systematic Review and Meta-Analysis. Matern Child Health J. 2022 Jul 1;26(7):1473–87.
16. Andrews NC. Anemia of inflammation: the cytokine-hepcidin link. J Clin Invest. 2004 May 1;113(9):1251–3.
17. Mbule MA, Byaruhanga YB, Kabahenda M, Lubowa A. Determinants of anaemia among pregnant women in rural Uganda. Rural and Remote Health. 2013 May;13(2):1–15.
18. McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. Public Health Nutr. 2009 Apr;12(4):444–54.

19. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. Lancet Glob Health. 2013 Jul;1(1):e16-25.
20. Milman N, Clausen J, Byg KE. Iron status in 268 Danish women aged 18-30 years: influence of menstruation, contraceptive method, and iron supplementation. Ann Hematol. 1998;77(1–2):13–9.
21. Aboagye RG, Okyere J, Seidu AA, Ahinkorah BO, Budu E, Yaya S. Relationship between history of hormonal contraceptive use and anaemia status among women in sub-Saharan Africa: A large population-based study. PLOS ONE. 2023 Jun 14;18(6):e0286392.
22. Haile ZT, Kingori C, Teweldeberhan AK, Chavan B. The relationship between history of hormonal contraceptive use and iron status among women in Tanzania: A population-based study. Sexual & Reproductive Healthcare. 2017 Oct 1;13:97–102.
23. Gebremedhin S, Asefa A. Association between type of contraceptive use and haemoglobin status among women of reproductive age in 24 sub-Saharan Africa countries. BMJ Sex Reprod Health. 2019 Jan 1;45(1):54–60.
24. Bellizzi S, Ali MM. Effect of oral contraception on anemia in 12 low- and middle-income countries. Contraception. 2018 Mar 1;97(3):236–42.
25. Milsom I, Andersson K, Jonasson K, Lindstedt G, Rybo G. The influence of the Gyne-T 380S IUD on menstrual blood loss and iron status. Contraception. 1995 Sep 1;52(3):175–9.
26. Rivera R, Yacobson I, Grimes D. The mechanism of action of hormonal contraceptives and intrauterine contraceptive devices. American Journal of Obstetrics and Gynecology. 1999 Nov 1;181(5):1263–9.
27. Sivasankaran S, Jonnalagadda S. Advances in controlled release hormonal technologies for contraception: A review of existing devices, underlying mechanisms, and future directions. Journal of Controlled Release. 2021 Feb 10;330:797–811.
28. Karra M, Canning D. The Effect of Improved Access to Family Planning on Postpartum Women: Protocol for a Randomized Controlled Trial. JMIR Research Protocols. 2020;9(8):e16697.
29. Karra M, Maggio D, Guo M, Ngwira B, Canning D. The causal effect of a family planning intervention on women's contraceptive use and birth spacing. Proc Natl Acad Sci USA. 2022 May 31;119(22):e2200279119.
30. National Statistical Office (NSO), ICF Macro. Malawi Demographic and Health Survey 2010. Zomba, Malawi and Calverton, MD: NSO and ICF Macro; 2011.
31. Vampire scare prompts U.N. pullout from southern Malawi. Reuters. 2017 Oct 9; Available from: https://www.reuters.com/article/us-malawi-un-vampires-idUSKBN1CE25E
32. Nakamura A, Nakamura M. On the Relationships Among Several Specification Error Tests Presented by Durbin, Wu, and Hausman. Econometrica. 1981;49(6):1583–8.
33. Greene WH. Econometric Analysis. 4th Edition. New Jersey: Pearson; 2000.
34. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva, Switzerland: World Health Organization; 2011.
35. Allison PD. Fixed Effects Regression Models. Thousand Oaks, Calif.: SAGE Publications; 2009. 167 p.

Figures and Tables

Figure 1: Histogram, Hemoglobin Levels (g/cL) in 2016 and 2018

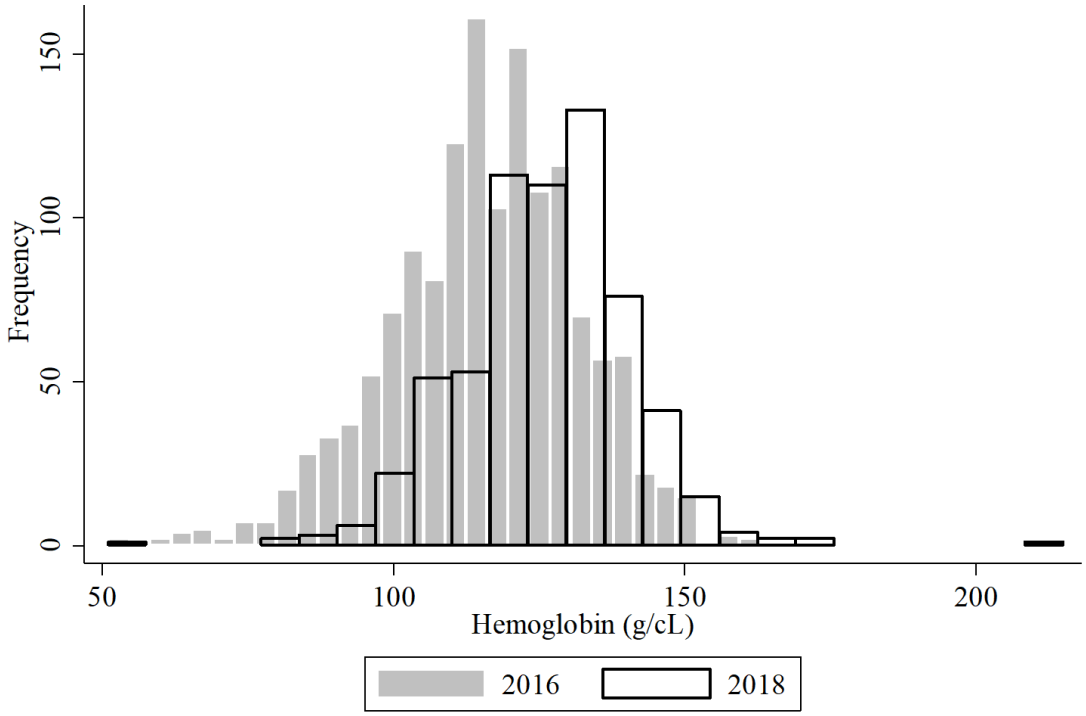


Table 1: Descriptive Statistics, by Survey Wave

	2016		2017		2018	
	Mean	SD	Mean	SD	Mean	SD
Outcomes						
Hemoglobin (g/cL)	110.196	17.278	125.767	15.272	126.054	14.559
Hemoglobin, Preg. Adjusted (g/cL)	115.628	16.351	125.958	15.191	126.431	14.442
Anemia Status						
None (adjusted greater than 120 g/cL)	0.430		0.695		0.709	
Low (adjusted between 110 and 120 g/cL)	0.243		0.186		0.172	
Moderate (adjusted between 80 and 110 g/cL)	0.307		0.112		0.118	
Severe (adjusted less than 80 g/cL)	0.020		0.008		0.002	
Anemic (1 = Yes)	0.570		0.305		0.291	
Covariates						
Currently Pregnant (1 = Yes)	0.543		0.137		0.038	
Currently Using FP (1 = Yes)	0.217		0.370		0.858	
Current Method Use						
None	0.783		0.163		0.142	
Female Sterilization	0.000		0.026		0.028	
IUD	0.001		0.008		0.008	
Injectable	0.173		0.572		0.499	
Implant	0.034		0.166		0.239	
Pills	0.003		0.036		0.054	
Condoms	0.006		0.018		0.017	
Standard Days Method	0.000		0.005		0.005	
Withdrawal	0.001		0.007		0.008	
Hormonal Method (1 = Yes)	0.210		0.774		0.792	
Educational Attainment						
None	0.568		0.525		0.523	
Primary	0.407		0.448		0.457	
Secondary	0.025		0.026		0.019	
Higher	0.000		0.001		0.002	
Currently working (1 = Yes)	0.086		0.190		0.227	
Owns agricultural land (1 = Yes)	0.347		0.320		0.301	
Age (years)	24.264	4.474	25.103	4.728	26.033	4.654
Total number of children	1.641	1.305	2.176	1.262	2.243	1.273
BMI	24.685	3.970	24.288	4.293	25.135	4.437
N	1447		1049		635	

Notes: The unit of observation is a woman. Standard deviations are presented for non-binary variables.

Table 2: Contraceptive Method Used and Hemoglobin Levels

	(1) Cross Section OLS	(2) Panel Fixed Effects	(3) Panel Random Effects
Outcome	Hemoglobin (g/cL)	Hemoglobin (g/cL)	Hemoglobin (g/cL)
Pregnancy Status (Ref: No)			
Pregnant (1 = Yes)	-6.745	-9.028***	-9.923***
	(-15.10 - 1.614)	(-13.37 - -4.690)	(-11.70 - -8.148)
Method Use (Ref: No Use)			
Female Sterilization	4.103	-1.214	-2.022
	(-2.671 - 10.88)	(-8.369 - 5.941)	(-6.924 - 2.879)
IUD	5.198	3.020	7.038*
	(-1.511 - 11.91)	(-7.898 - 13.94)	(-1.116 - 15.19)
Injectable	4.742**	1.570	3.684***
	(0.0125 - 9.471)	(-0.681 - 3.822)	(2.060 - 5.309)
Implant	7.285***	3.828**	5.705***
	(2.259 - 12.31)	(0.644 - 7.012)	(3.532 - 7.878)
Pill	1.783	-1.197	2.169
	(-5.299 - 8.866)	(-5.977 - 3.583)	(-1.519 - 5.856)
Condom	-0.638	-0.504	-0.219
	(-9.589 - 8.314)	(-7.774 - 6.766)	(-5.300 - 4.861)
Standard Days	8.142	-1.578	3.283
	(-4.621 - 20.91)	(-17.31 - 14.15)	(-7.218 - 13.78)
Withdrawal	-0.154	1.216	2.625
	(-12.50 - 12.19)	(-9.152 - 11.58)	(-5.519 - 10.77)
Constant	118.5***	107.7***	108.5***
	(106.8 - 130.2)	(95.30 - 120.1)	(104.7 - 112.3)
Test of Fixed Effect versus Random Effect models			
Wu-Hausman F-statistic (p-value)		15.26 (0.4325)	
Observations	635	3,131	3,131
Number of Women	635	1,732	1,732
R-squared	0.155		

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Notes: For all columns, the unit of observation is a woman. Column 1 presents OLS results from an adjusted linear model using the wave 3 cross-sectional data, with 95 percent confidence intervals in parentheses. Columns 2 and 3 respectively present results from adjusted panel woman fixed effects (FE) and woman random effects (RE) regression models with 95 percent confidence intervals in parentheses. Time-varying covariates in all models include the total number of children ever born, whether the woman works, the woman's BMI, and whether the woman's household owns any agricultural land. Time-invariant covariates in the OLS model include the woman's educational attainment (none, primary, secondary, or higher), age of the woman (in completed years), and her ever use of contraception. For the OLS model, area and survey wave fixed effects are included, and heteroscedasticity-robust standard errors are presented in all regressions. For the panel FE and RE models, survey wave fixed effects are included in all regressions.

Table 3: Test of Parameter Equality on Methods for Fixed Effect and Random Effect Models

	FE	RE	Diff. (FE – RE)	SE	Test Statistic
Comparison of coefficients Table 3, Columns 2 and 3					
Pregnant (1 = Yes)	-9.028	-9.923	0.895	2.01	0.445
Current Method Use					
Female Sterilization	-1.214	-2.022	0.808	2.64	0.306
IUD	3.02	7.038	-4.018	3.671	-1.095
Injectable	1.57	3.684	-2.114	0.789	-2.679**
Implant	3.828	5.705	-1.877	1.178	-1.593
Pills	-1.197	2.169	-3.366	1.536	-2.191**
Condoms	-0.504	-0.219	-0.285	2.632	-0.108
Standard Days Method	-1.578	3.283	-4.861	5.934	-0.819
Withdrawal	1.216	2.625	-1.409	3.24	-0.435
Currently working (1 = Yes)	0.579	0.694	-0.115	0.73	-0.158
Owns agricultural land (1 = Yes)	-0.474	-0.444	-0.03	0.691	-0.043
BMI	0.149	0.275	-0.125	0.155	-0.806
Total number of children	2.189	-0.261	2.451	2.095	1.17
Survey Wave					
2017	8.158	8.089	0.069	0.59	0.117
2018	8.556	8.287	0.269	0.711	0.378
Wu-Hausman F-Statistic (p-value)	15.26 (0.4325)				

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 4: Hormonal Contraceptive Use and Hemoglobin Levels

	(1) Cross Section OLS	(2) Panel Fixed Effects	(3) Panel Random Effects
Outcome	Hemoglobin (g/cL)	Hemoglobin (g/cL)	Hemoglobin (g/cL)
Pregnancy Status (Ref: No)			
Pregnant (1 = Yes)	-6.978*	-9.052***	-9.988***
	(-15.26 - 1.299)	(-13.37 - -4.730)	(-11.76 - -8.217)
Method Use (Ref: No Use)			
Non-Hormonal Method (1 = Yes)	2.135	-0.239	0.251
	(-3.394 - 7.664)	(-4.761 - 4.283)	(-2.985 - 3.487)
Hormonal Method (1 = Yes)	4.931**	1.729	3.917***
	(0.466 - 9.397)	(-0.452 - 3.911)	(2.350 - 5.483)
Constant	118.3***	108.0***	108.7***
	(106.9 - 129.8)	(95.62 - 120.4)	(104.9 - 112.5)
Test of Fixed Effect versus Random Effect models			
Wu-Hausman F-statistic (p-value)		20.97 (0.0.0128)	
Observations	635	3,131	3,131
Number of Women		1,732	1,732
R-squared	0.144		

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Notes: For all columns, the unit of observation is a woman. Column 1 presents OLS results from an adjusted linear model using the wave 3 cross-sectional data, with 95 percent confidence intervals in parentheses. Columns 2 and 3 respectively present results from adjusted panel woman fixed effects (FE) and woman random effects (RE) regression models with 95 percent confidence intervals in parentheses. Time-varying covariates in all models include the total number of children ever born, whether the woman works, the woman's BMI, and whether the woman's household owns any agricultural land. Time-invariant covariates in the OLS model include the woman's educational attainment (none, primary, secondary, or higher), age of the woman (in completed years), and her ever use of contraception. For the OLS model, area and survey wave fixed effects are included, and heteroscedasticity-robust standard errors are presented in all regressions. For the panel FE and RE models, survey wave fixed effects are included in all regressions.

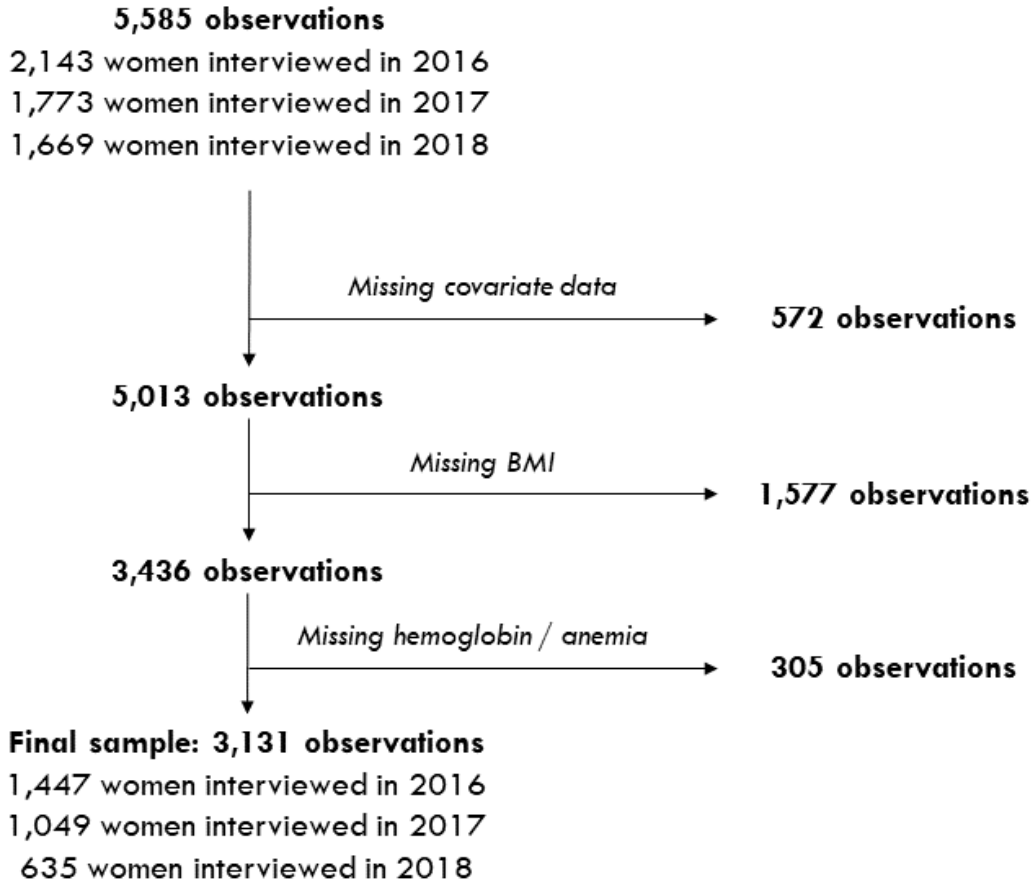
Table 5: Test of Parameter Equality on Hormonal method use for Fixed Effect and Random Effect Models

	FE	RE	Diff. (FE – RE)	SE	Test Statistic
Comparison of Table 5, Columns 2 and 3					
Pregnant (1 = Yes)	-0.129	0.172	-0.301	0.376	-0.801
Current Method Use (Ref: No Use)					
Use Non-Hormonal Method	-0.119	0.103	-0.222	0.411	-0.54
Use Hormonal Method	-0.144	-0.492	0.348	0.162	2.148**
Currently working (1 = Yes)	-0.361	-0.183	-0.178	0.166	-1.072
Owns agricultural land (1 = Yes)	0.188	0.026	0.162	0.158	1.025
BMI	-0.03	-0.046	0.016	0.033	0.485
Total number of children	-0.568	0.052	-0.621	0.381	-1.63
Survey Wave					
2017	-0.92	-1.015	0.095	0.121	0.785
2018	-1.082	-1.086	0.005	0.144	0.035
Wu-Hausman F-Statistic (p-value)	20.97 (0.0128)				

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Appendix

Appendix Figure 1: Sample Flowchart



Note: An observation refers to a woman-year (e.g. a woman i interviewed in year j).