

GYNECOLOGY

Risk factors for and outcomes of ring expulsions with a 1-year contraceptive vaginal system



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BACKGROUND: The US Food and Drug Administration—approved segesterone acetate and ethinyl estradiol ring-shaped contraceptive vaginal system, known as Annovera (Sever Pharma Solutions/QPharma, Malmö, Sweden), was inserted and removed under a woman's control for a 21 day in and 7 day out regimen for up to 13 cycles of use.

OBJECTIVE: We aimed to describe the patterns of ring expulsion over time, to identify potential predictors of expulsion, and to evaluate the impact of expulsions on method discontinuation and pregnancy risk.

STUDY DESIGN: Using data from 2064 participants who were enrolled in 2 multinational phase 3 clinical trials on the use of this contraceptive vaginal system, we examined data from participants' daily diaries for documentation of complete ring expulsion. We modeled the odds of reported expulsions over time with adjustment for background and demographic characteristics using mixed-effects logistic regression models with random intercepts. We compared the probability of continuation between those who did and those who did not report expulsions in the first cycle of use using survival analysis and hazards modeling. To determine if expulsions during the first cycle of use affected the risk for pregnancy, we calculated Pearl Indices.

RESULTS: Most participants (75%) never experienced any expulsions during any cycle of use, and 91% to 97% did not experience an expulsion during any 1 cycle. The incidence of expulsion was highest in cycle 1 (9%). The odds of experiencing expulsions decreased by half in cycles 2 to 8 when compared with cycle 1 (0.48; 95% confidence interval, 0.40–0.58), and in cycles 9 to 13, expulsions were about a third of that in cycle 1 (0.32; 95% confidence interval, 0.26–0.41). Of those who did experience expulsions, most (62%–84%) experienced ≤ 2

expulsions per cycle. Participants from study sites in Latin America vs those in the United States had higher odds of not experiencing an expulsion (odds ratio, 1.95; 95% confidence interval, 1.45–2.63). Women with a higher education level had higher odds of experiencing an expulsion. Notably, parity, age, and body mass index were not associated with expulsion.

Participants who experienced any expulsions in cycle 1 were more likely to discontinue use early (hazard ratio, 1.28; 95% confidence interval, 1.14–1.43) than participants who did not have an expulsion. The Pearl Index for participants who had expulsions during cycle 1 was 3.99 (95% confidence interval, 1.29–9.31), which was higher than that among participants who reported no expulsions (Pearl Index, 2.39; 95% confidence interval, 1.61–3.41), but the overlapping confidence intervals indicate that there is not sufficient evidence to demonstrate an association between expulsions and pregnancy risk.

CONCLUSION: Expulsions were infrequent overall, decreased with subsequent cycles of use, and were not associated with body mass index or parity. Early discontinuation of product use was higher among participants who experienced an expulsion during cycle 1. Although it is unclear whether pregnancy risk was associated with expulsions, early recognition of expulsions among users may identify those at higher risk for discontinuation and may highlight when enhanced anticipatory counselling and guidance may be advantageous.

Key words: acceptability, Annovera, contraception, counseling, discontinuation, Nestorone, Pearl Index, pregnancy, segesterone acetate, vaginal ring

Introduction

The Population Council developed a ring-shaped contraceptive vaginal system (CVS) that releases the progestin segesterone acetate (SA)—also known as Nestorone—and ethinyl estradiol (EE) and that is used continuously in a regimen of 21 days in and 7 days out for up to 13 menstrual cycles.^{1–3} In 2018, this CVS, known as Annovera (Sever Pharma

Solutions/QPharma, Malmö, Sweden) was approved by the US Food and Drug Administration. It is safe and effective with a Pearl Index of 2.98 (95% confidence interval [CI], 2.13–4.06).^{3–5} Similar to other vaginal rings, the SA+EE CVS is a discreet and user-controlled option that individuals can insert and remove themselves at any time to discontinue use. The CVS provides the novel benefit of lasting a full year without requiring a trained provider for insertion or removal.

The goal of contraceptive development is to create safe and effective methods that users find acceptable, that are convenient and easy to use, and that has high user satisfaction and continuation. This, in turn, increases effective and

continued use and reduces the risk for unintended pregnancy. For the SA+EE CVS, 4 key acceptability domains have been identified previously, namely ease of use, effect on sexual function, perceived side effects, and experiences related to expulsions or feeling the ring.⁴ In this manuscript, we focus on the impact of ring expulsions (ring coming out of the vagina involuntarily) on method continuation and pregnancy incidence.

Across the phase 3 trials for the SA+EE CVS, 25% of participants experienced at least 1 complete expulsion during the study, and 44% experienced at least 1 partial expulsion, although discontinuation owing to expulsions was relatively low (1.4%).⁵ Participants who

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AJOG at a Glance

Why was this study conducted?

We aimed to describe patterns of ring expulsion over time, to identify potential predictors of expulsion, and to evaluate the impact of expulsions on method discontinuation and pregnancy risk.

Key findings

Expulsions were rare and decreased with use and were less commonly documented by users at Latin American sites or with lower education. Users who experienced expulsions during the first cycle of use were more likely to discontinue use early.

What does this add to what is known?

Expulsions are an established component of ring acceptability. Our study suggests that the timing of expulsions—specifically during the first cycle of use—may impact acceptability and in turn continuation, which has implications for counseling.

experienced ≤ 1 expulsion per week had 3.4 times the odds of being satisfied with the CVS when compared with those who had > 1 expulsion per week.⁴ Given these findings and the fact that users may be concerned about potential expulsions,⁶ we aimed to identify baseline risk factors for expulsions, to explore patterns of expulsions with SA+EE CVS use over time, and to evaluate the impact of expulsions on method discontinuation and pregnancy. A better understanding of the risk factors for and trends in expulsions over time gives providers important data to enhance anticipatory counseling and, ultimately, to enhance user satisfaction.

Materials and Methods

We performed a secondary analysis of diary data obtained during 2 identically designed, multicenter, open-labeled, single-arm, phase 3 trials of the SA+EE CVS registered with [ClinicalTrials.gov](https://clinicaltrials.gov) under identifiers NCT00455156 and NCT00263341. Study protocols were approved by the institutional review boards (IRBs) of the Population Council and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Coordinating Center and by the IRB or ethics committee at each site. All potential participants provided written informed consent before screening and initiation of any study procedures. Detailed methods and results have been described previously.⁵

Participants followed a regimen in which the CVS was to be kept in the vagina continuously for 21 days, followed by 7 days without the device for up to 13 cycles. Participants recorded daily in paper diaries whether they experienced a complete, partial, or no expulsion. Complete expulsion was defined as the CVS coming out of the vagina completely; a partial expulsion was defined as the CVS moving out of place, but not coming out of the vagina completely. We excluded partial expulsions from this analysis because they are a more subjective experience than complete expulsions. The clinical significance of partial expulsions is unclear, and the reporting may lack objectivity, whereas complete expulsions can impact the effectiveness of the device depending on how long it is out of the vagina. We based our analysis on the Merkatz⁴ acceptability framework, which posits that the acceptability domains of ease of use, side effects, effects on sex, and expulsions impact satisfaction and, in turn, influence adherence and method continuation. We sought to determine if experiencing an expulsion or frequent expulsions in cycle 1 was associated with the risk for pregnancy or discontinuation.

Statistical analysis

Consistent with other analyses using diary data from these studies, our

analysis population included participants who completed their diary entry for at least 15 days during at least 1 of their cycles of ring use.⁷ Missing data were not imputed; if a participant did not submit a completed diary for a given cycle, that cycle was not included in the analysis for that participant. Using Pearson's chi-square tests, we summarized and compared the demographic and background characteristics of participants who ever experienced a complete expulsion during their study participation and those who did not experience a complete expulsion. We explored the pattern of expulsions over the course of ring use by examining the proportion of participants who experienced no expulsions and those who experienced 1, 2, 3, or frequent (≥ 4) expulsions by cycle of use. To determine how occurrence of expulsions changed by cycle of ring use, we modeled the probability of experiencing an expulsion by cycle of ring use, grouping cycles into 3 categories, namely cycle 1, cycles 2 to 8, and cycles 9 to 13, using a simple mixed-effects logistic regression model with random intercepts because of repeated measures among participants. In addition, we modeled the probability of experiencing an expulsion using mixed-effects logistic regression models for demographic characteristics that were associated with expulsion in the bivariate model ($P < .05$). We examined cycle and demographic effects on expulsion in both unadjusted (bivariate) models and altogether in an adjusted model.

We calculated Pearl Indices with 95% CIs for participants who had no expulsions, those who had ≥ 1 expulsions, those who had ≤ 3 expulsions; and those who had ≥ 4 expulsions. For this analysis, we considered only expulsions that occurred during cycle 1 because expulsions during the first cycle of use may impact risk factors for pregnancy (such as adherence) in subsequent cycles and because the first cycle is when counseling on product use could be the most impactful.

To describe the relationship between expulsions and early discontinuation (discontinuing before the end of the study), we plotted Kaplan-Meier survival

curves for the probability of continuing in the analysis of participants who had no expulsions in cycle 1 vs those who had ≥ 1 expulsions in cycle 1, conducted log-rank tests, and computed the hazard ratios with 95% CIs. We also plotted survival curves for participants who had ≤ 3 expulsions in cycle 1 vs those who had ≥ 4 expulsions in cycle 1 and computed the hazard ratios with 95% CIs. In the survival analyses, participants were censored if they completed the study or if they discontinued for a reason not related to ring use (eg, change in eligibility criteria). Similar to the analysis of expulsion and pregnancy, we focused only on expulsions during cycle 1, because we hypothesized that an expulsion during the first cycle of use may be related to latent factors that affect continuation and study participation and it is an optimal time for targeted counseling.

Results

There were 2064 participants included in our analysis. Most participants (1810/2064) had complete diary data; only 13% were missing diary entries for >2 cycles. Overall, 25% of participants ever experienced an expulsion during any cycle of participation in the study. Among those who did experience an expulsion, it only occurred once in most cases (48%–60% of participants). Very few participants (1.5%) experienced ≥ 4 expulsions in any one cycle. Only 2 participants experienced daily expulsions in a cycle, occurring in cycle 1 and the other in cycles 4 to 5. When expulsions occurred, they were brief. In 90% of cycles when an expulsion occurred, diary entries indicated that the ring was never out (>2 hours/day) on the day of or following the expulsion. Approximately half (1064) of participants were administered an acceptability questionnaire at the last cycle of use, which included a question about their activity when complete or partial expulsions occurred. A total of 56% reported that the expulsion occurred during a bowel movement, 37% reported that it occurred during exercise, and 4% reported that it occurred during sexual intercourse. In addition, among participants who were

administered acceptability questionnaires, the reported satisfaction was similar among those with and without expulsion with 88% of participants who ever reported expulsion vs 86% who never reported an expulsion saying that they were satisfied or very satisfied at the end of the study ($P=.53$).

Participants who experienced any expulsions were more likely to be non-Hispanic, from a US study site, or a college graduate. There was insufficient evidence of differences in expulsions by age, race, parity, or body mass index (BMI). Baseline characteristics by expulsion status are shown in [Table 1](#).

The number of participants who experienced any expulsions decreased with each subsequent cycle as shown in [Figure 1](#). For example, in cycle 1, 9% of participants experienced expulsions, in cycle 6, 4% of participants experienced expulsions, and in cycle 13, 3% of participants experienced expulsions. The rates of participants who experienced multiple expulsions in a cycle also decreased as time progressed but plateaued around cycle 6.

The odds of experiencing an expulsion were significantly lower after cycle 1 as detailed in [Table 2](#). The odds of experiencing expulsions decreased by half in cycles 2 to 8 when compared with cycle 1 (0.48; 95% CI, 0.40–0.58), and in cycles 9 to 13, expulsions were about a third of that in cycle 1 (0.32; 95% CI, 0.26–0.41).

Ethnicity, education, and study site were each individually associated with expulsion. However, because of collinearity between these covariates, in the adjusted regression model, study site remained a strong predictor of expulsion, along with education and cycle of use. Participants at sites in Latin America, when compared with those in the United States, had lower adjusted odds of reporting an expulsion (odds ratio [OR], 0.49; 95% CI, 0.36–0.66). In the adjusted model, education level increased the likelihood of reporting an expulsion; participants with only a grade school education were the least likely to have reported an expulsion.

To assess whether differences in diary completion between different groups

explained the differences in expulsion rate among demographic groups, we performed a subgroup analysis that was limited to only those participants who had no missing diary data. The trends seen with the full sample had similar adjusted ORs. There were higher odds of expulsions among those in the United States than among those in Latin America, and it was also higher among those with higher education.

Among participants who reported any expulsions during cycle 1, 5 became pregnant during the study, corresponding to a Pearl Index of 3.99 (95% CI, 1.29–9.31) and compared with a Pearl Index of 2.39 (95% CI, 1.61–3.41) among participants who did not report any expulsions during cycle 1. No pregnancies occurred among the 29 participants who had frequent expulsions (≥ 4) during cycle 1.

Experiencing an expulsion during the first cycle of ring use was associated with early discontinuation of use and exit from the study. The Kaplan-Meier estimated cumulative probability of discontinuing use early among participants who had no expulsions in cycle 1 was 26% compared with 31% among participants who had ≥ 1 expulsion in cycle 1. The corresponding survival curves (representing continuation in the study) were different with a log-rank P value of $<.0001$. The hazards model estimated that participants who had any expulsions in cycle 1 were 28% more likely to discontinue use (hazard ratio, 1.28; 95% CI, 1.14–1.43), however, it may be possible that this hazard ratio (increased risk) may not be constant throughout the whole year of use. We observed a larger difference in the survival curves between participants who had frequent (≥ 4) expulsions in the first cycle and those who had ≤ 3 expulsions (log-rank P value of $<.0001$). Women who experienced frequent (≥ 4) expulsions in cycle 1 were more than twice as likely to discontinue use early (hazard ratio, 2.40; 95% CI, 1.93–2.98) than participants who had ≤ 3 expulsions during the first cycle. The survival curves are shown in [Figures 2 and 3](#).

To explore whether the decrease in expulsion occurrence over time was

TABLE 1
Participant characteristics by expulsion experienced during the study

| Characteristic | No expulsions (ever) | Expulsion (ever) | Chi-square <i>P</i> value | No expulsion in cycle 1 | Expulsion in cycle 1 | Chi-square <i>P</i> value |
|--------------------------|----------------------|------------------|------------------------------|-------------------------|----------------------|------------------------------|
| | n (%) | n (%) | | n (%) | n (%) | |
| Total | 1557 (75.4) | 507 (24.6) | | 1836 (91) | 187 (9) | |
| Age (y) | | | .93 | | | .36 |
| 18–19 | 90 (5.8) | 31 (6.1) | | 105 (5.7) | 15 (8.0) | |
| 20–24 | 586 (37.6) | 183 (36.1) | | 690 (37.6) | 67 (35.8) | |
| 25–29 | 510 (32.8) | 169 (33.3) | | 607 (33.1) | 53 (28.3) | |
| 30–35 | 272 (17.5) | 87 (17.2) | | 316 (17.2) | 36 (19.3) | |
| >36 | 99 (6.4) | 37 (7.3) | | 118 (6.4) | 16 (9.24) | |
| Race | | | .47 | | | .13 |
| White | 1118 (71.8) | 378 (74.6) | | 1323 (72.1) | 145 (77.5) | |
| Black | 215 (13.8) | 65 (12.8) | | 250 (13.6) | 25 (13.4) | |
| Other | 224 (14.4) | 64 (12.6) | | 263 (14.3) | 147 (9.1) | |
| Ethnicity | | | .0075 | | | .0116 |
| Hispanic | 471 (30.2) | 122 (24.1) | | 544 (30) | 39 (21) | |
| Not Hispanic | 1086 (69.8) | 385 (75.9) | | 1292 (70) | 148 (79) | |
| Parity | | | .21 | | | .57 |
| Nulliparous | 1008 (64.7) | 347 (68.4) | | 1197 (65.2) | 129 (70.0) | |
| Parous (P=1) | 255 (16.4) | 81 (16.0) | | 306 (16.7) | 27 (14.4) | |
| Parous (P≥2) | 294 (18.9) | 79 (15.6) | | 333 (18.1) | 31 (16.6) | |
| BMI | | | .25 | | | .07 |
| <29 | 1441 (92.7) | 460 (91.1) | | 1695 (92.5) | 166 (88.8) | |
| >29 | 114 (7.3) | 45 (8.9) | | 137 (7.5) | 21 (11.2) | |
| Education | | | .001 | | | .08 |
| Grade school | 113 (7.3) | 15 (3.0) | | 120 (6.5) | 6 (3.2) | |
| High school Graduate | 301 (19.3) | 77 (15.2) | | 334 (18.2) | 36 (19.3) | |
| Some college | 493 (31.7) | 178 (35.1) | | 607 (33.1) | 52 (27.8) | |
| College graduate or more | 650 (41.8) | 237 (46.8) | | | | |
| Site | | | .0005 | | | .07 |
| Latin America | 291 (18.7) | 59 (11.6) | | 325 (17.7) | 21 (11.2) | |
| Europe and Australia | 281 (18.1) | 86 (17.0) | | 325 (17.7) | 38 (20.3) | |
| United States | 985 (63.3) | 362 (71.4) | | 1186 (64.6) | 128 (68.5) | |

Plagianos. Expulsions with a 1-year contraceptive vaginal system. *Am J Obstet Gynecol* 2024.

driven by attrition among participants who had expulsions, we conducted a sensitivity analysis of the mixed methods regression with inclusion of only participants who did not discontinue use early. The results were similar to the overall mixed methods model with a 55% reduction in expulsions in cycles 2 to 8 when compared with cycle 1 and a

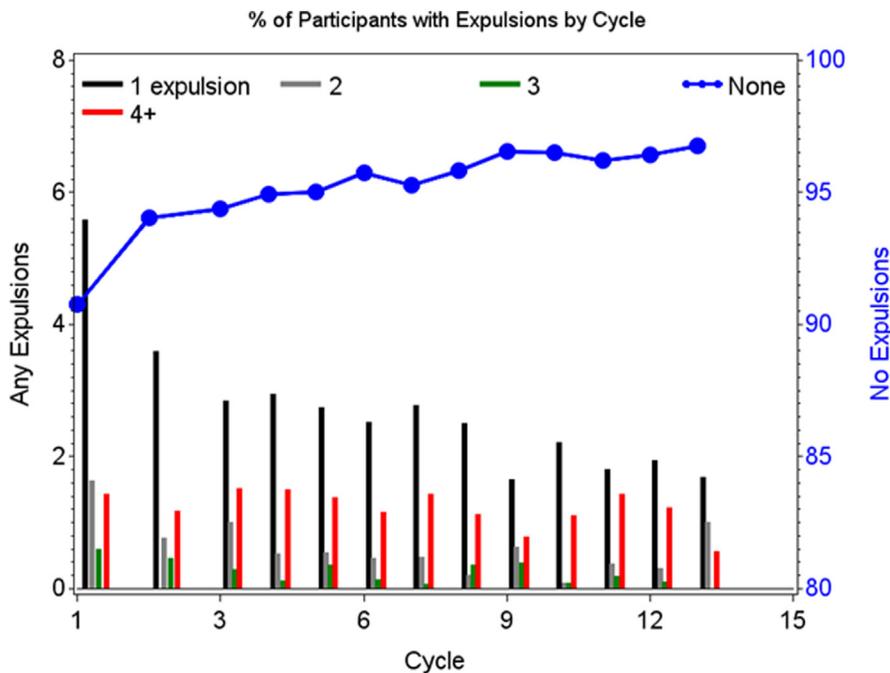
65% reduction in cycles 9 to 13 when compared with cycle 1.

Comment Principal findings

Overall, most (75%) users of the SA+EE CVS never experienced any complete expulsions during participation in the study. Furthermore, the risk for

expulsion decreased significantly with longer use. Participants with a lower education level and those who were from Latin American sites were less likely to have reported expulsions. We also found that when participants experienced an expulsion during their first cycle of use, they were more likely to discontinue use early.

FIGURE 1
Participants experiencing any expulsions, and no expulsions by cycle



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Results in the context of what is known

Although expulsions occur with vaginal rings, this study showed that they are

infrequent and decrease with time, which has been observed with different types of vaginal rings in different populations, including the HIV Preexposure

prophylactic Dapivirine ring that is used by women in Sub-Saharan African and a contraceptive vaginal ring that is used by lactating women.^{8–10} Although only 1% of participants in our studies discontinued use early because of frequent expulsions,⁵ those who experienced an expulsion during the first cycle of use had increased odds of study discontinuation for any reason. Similarly, for the contraceptive vaginal ring used by lactating women in Sub-Saharan Africa and India, the expulsion rates were higher among users who discontinued use early.^{8,10}

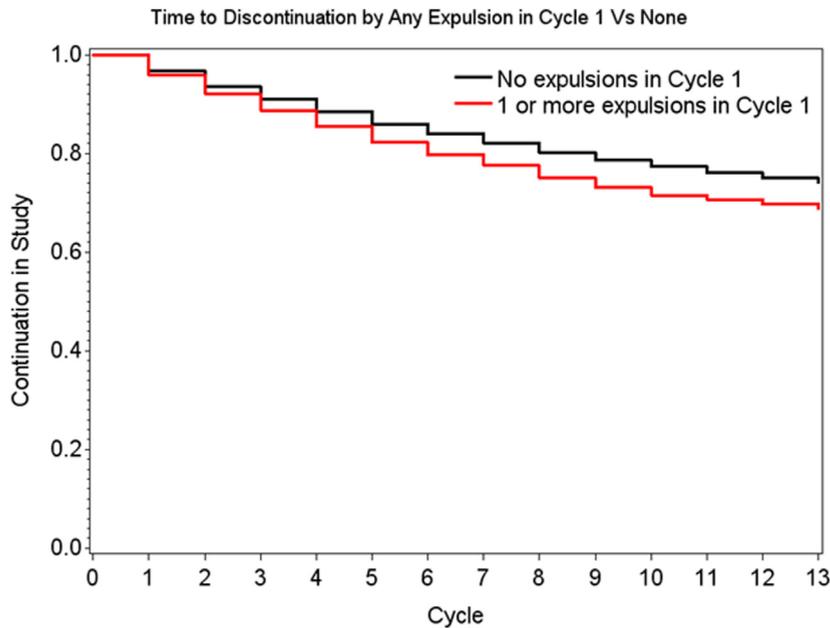
Expulsion experience varied by geographic region¹¹ and occurred more frequently in the Americas than in Europe; data from our study revealed that fewer reported expulsions at Latin American sites than in the United States. Although results from several other studies described that parous users were more likely to experience expulsions,¹¹ we did not observe differences in expulsions by parity. Differences in the physical ring characteristics and variation in the anatomy among ring users can contribute to expulsions,^{11,12} which may explain why our findings are different from those of expulsion analyses of other types of vaginal rings.

TABLE 2
Mixed-effects logistic regression modeling of the probability of expulsion by cycle

| Characteristic | Unadjusted odds ratio (95% confidence interval) | Type 3 F-test P value (unadjusted models) | Adjusted odds ratio (95% confidence interval) | Type 3 F-test P value (adjusted model) |
|--------------------------------------|---|---|---|--|
| Cycle of use | | <.0001 | | <.0001 |
| Cycle 2–8 vs cycle 1 | 0.48 (0.40–0.58) | | 0.48 (0.40–0.58) | |
| Cycle 9–13 vs cycle 1 | 0.32 (0.26–0.41) | | 0.33 (0.26–0.42) | |
| Study site location | | <.0001 | | .0158 |
| Europe or Australia vs United States | 0.93 (0.72–1.21) | | 1.00 (0.76–1.31) | |
| Latin America vs United States | 0.49 (0.36–0.66) | | 0.55 (0.37–0.83) | |
| Ethnicity | | .0028 | | .47 |
| Hispanic vs non-Hispanic | 0.70 (0.56–0.89) | | 1.12 (0.82–1.54) | |
| Education | | .0007 | | .0468 |
| High school vs grade school | 2.29 (1.26–4.19) | | 2.09 (1.14–3.83) | |
| Some college vs grade school | 2.89 (1.62–5.15) | | 2.27 (1.25–4.13) | |
| College graduate vs grade school | 3.04 (1.72–5.39) | | 2.36 (1.30–4.31) | |

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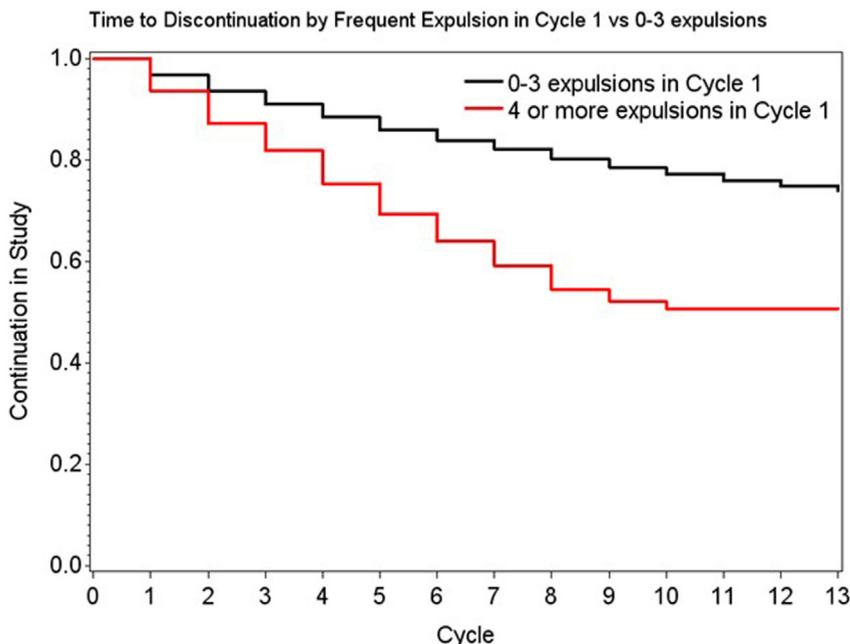
FIGURE 2
Time to discontinuation by any expulsion in cycle 1 vs no expulsion in cycle 1



Survival curve for time to discontinuation for participants who had any expulsion in cycle 1 and for those who had no expulsions in cycle 1.

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FIGURE 3
Time to discontinuation by frequent (≥ 4) expulsions in cycle 1 vs 0 to 3 expulsions in cycle 1



Survival curve for time to discontinuation among participants who had frequent expulsions (≥ 4) in cycle 1 and for those who had 0 to 3 expulsions in cycle 1.

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Clinical implications

Because frequent expulsions occur in a small proportion of individuals, directive, early counseling to identify if placement is the issue may help to reduce the expulsion risk. Given our findings that expulsions in the first cycle of use were associated with a higher risk for early discontinuation, it is critical for providers to counsel patients on the proper placement of the ring and to provide reassurance that even if expulsions occur, the frequency of expulsions is likely to decrease over time as seen in our data. Anticipatory counseling by providers will empower users to continue use of this method, and this will improve overall satisfaction. In addition, it is possible that those who experienced frequent expulsions may benefit from early counseling on alternative options to reduce the risk for method discontinuation without an alternative readily available.

It is worth noting that parity was not associated with expulsion risk, nor were race or BMI. These findings indicate that potential users across various demographic backgrounds are likely to be successful in using the contraceptive vaginal ring.

Research implications

Of note, the Pearl Indices calculated for each group had overlapping confidence intervals, and thus, having a more extensive study on the pregnancy rates among a larger group of ring users who experienced complete expulsions could help to further clarify the true pregnancy risk. Although it is unlikely that a brief (<2 hour) expulsion alone would affect efficacy, expulsions are a component of acceptability and acceptability⁴ affects adherence.¹³ The occurrence of expulsions may impact user adherence and, in time, impact efficacy. Additional research is needed to determine whether or how expulsions may affect the risk for unintended pregnancy.

This study relied on participants documenting, in paper diaries, the occurrence of ring expulsions during each day of use and returning their diaries to the study site at scheduled quarterly visits. Data collection on

expulsions and other user-reported outcomes may be improved with daily text messaging or via smart phone applications with daily or weekly reminders.

Ongoing research studies that are being conducted by the Population Council include collecting data from qualitative and quantitative interviews and collecting daily reports of expulsion and ring removal via text message. This may further clarify the characteristics of users who experienced expulsions with rings and potentially related outcomes from expulsions.

For future studies focused on expulsions, additional methods for identifying expulsions would be helpful. Alternatively, if objective monitors of adherence, such as temperature sensors or biomarkers could be leveraged, more accurate data could be obtained and better detail regarding the frequency and nature of removals and expulsions could be captured.

Strengths and limitations

The strengths of this study include its large sample size and diverse populations from the United States, Europe, and Latin America and the detailed daily data on expulsions collected from participants for up to 1 year of use. Our analyses that focused on expulsion during the first cycle of use are easy to interpret and furnish providers with pertinent messaging for effective counseling early on. However, we recognize that models that use time-varying predictors could provide more comprehensive information.

This study has a number of limitations. The use of diaries that require daily notations or rely on participant recollection can be challenging and may lead to imprecise data. Our sensitivity analysis on the subset of participants who did not have missing diary data yielded results that were similar to the overall results, supporting that there were minimal differences between participants with and those without missing diary data. However, it is possible that there were demographic differences in the reporting of expulsions in the diaries, including differences in education level

or geographic location of the study sites, leading to the observation of more expulsions among some groups. In other words, the observed differences in expulsions by demographic groups could have been caused by a difference in reporting and not by a difference in actual expulsion events. In the same trial, diary reports of unscheduled bleeding were also highest among participants with higher levels of education.⁷ It is possible that participants with higher education may have been more likely to properly record expulsion and bleeding events in their diaries. Some of the differences in documentation of the expulsions we found may also be explained by social desirability bias; participants with less education or from different cultural backgrounds may want to please providers and research staff by not reporting complications like expulsions.

Conclusion

In the phase 3 trials, expulsion of the SA+EE CVS was a rare event, and the occurrence of expulsions decreased over time. Noting the importance of anticipatory counseling regarding vaginal ring use, we recommend counseling new users about expulsions and informing them that if expulsions occur, the incidence thereof will likely decrease over subsequent cycles. Such information may enhance users' overall satisfaction with the method, reduce the risk for early discontinuation, and, in turn, support patients' successful use of this important contraceptive method. ■

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The first clinical trial was registered with [ClinicalTrials.gov](https://clinicaltrials.gov) under identifier NCT00263341 on December 8, 2005, and the first participant was enrolled on November 25, 2006. The registration site URL is <https://clinicaltrials.gov/ct2/show/NCT00263341>.

The second clinical trial was registered with [ClinicalTrials.gov](https://clinicaltrials.gov) under identifier NCT00455156 on April 3, 2007, and the first participant was enrolled on January 3, 2007. The registration site URL is <https://clinicaltrials.gov/ct2/show/NCT00455156>.

Individual participant data that underlie the results reported in this article and supporting metadata will be made available upon request to researchers who

contact the corresponding author at mplagianos@popcouncil.org with a methodologically sound proposal for analysis.

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