**Exploring menstrual products: a systematic review and meta-analysis of menstrual cups for public health internationally**

**Authors**

Anna Maria van Eijk, PhD1

Garazi Zulaika, MPH1

Madeline Lenchner, MSc2

Linda Mason, PhD1

Muthusamy Sivakami, PhD3

Elizabeth Nyothach, MSc4

Holger Unger, PhD5

Kayla Laserson, ScD6

Penelope A. Phillips-Howard, PhD1

**Affiliations**

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| 1 | Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool L3 5QA, United Kingdom |
| 2 | Departments of Biology and Health: Science, Society, and Policy, Brandeis University, Waltham, MA 02453, USA |
| 3 | Centre for Health and Social Sciences, School of Health Systems Studies, Tata Institute of Social Sciences, Mumbai, Maharashtra 400088, India |
| 4 | Centre for Global Health Research, Kenya Medical Research Institute (KEMRI), Kisumu, Kenya |
| 5 | Department of Obstetrics and Gynaecology, Edinburgh Royal Infirmary, Edinburgh EH16 4SA, United Kingdom and Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine, Liverpool L3 5QA, United Kingdom |
| 6 | Bill and Melinda Gates Foundation, India Country Office, New Delhi, India |

**aCorrespondence**

Dr. Penelope Phillips-Howard, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK. Tel: +44(0)7985431005 (UK); +254 702126188 (Kenya). Email: Penelope.Phillips-Howard@lstmed.ac.uk

**Short title: A systematic review of menstrual cups**

**Abbreviations**

HIC: High income countries

LMIC: Low and middle-income countries

MC: Menstrual cup

TSS: Toxic shock syndrome

TSST-1: Toxic shock syndrome toxin-1

**Abstract**

**Background**

Girls and women need effective, safe, and affordable menstrual products. Single-use products are regularly selected by agencies for resource-poor settings. The menstrual cup (MC) is a less-known alternative. We reviewed international studies on MC leakage, acceptability, and safety and explored MC availability to inform programmes.

**Methods**

We searched ten databases through 14 May 2019 for quantitative or qualitative studies on experiences and leakage associated with MCs, and adverse event reports. Results were tabulated or combined using forest plots (random-effects meta-analysis). Global availability and inclusion of MCs in international websites on menarche were explored.

**Findings**

Of 436 records, 43 studies were included (3319 participants). The main outcome of leakage was reported in four studies (293 women) only and was similar or lower for MCs compared with disposable pads or tampons. The adoption of MC required a familiarisation phase over cycles (four studies); peer support improved uptake (two studies in developing countries). In 15 studies, 73% (pooled estimate) of participants (95% CI 59-84%, *I2* 96%, N=1144) wished to continue use at study completion. MC-use showed no adverse effects on the vaginal flora (4 studies, 507 women). We identified five cases/reports within studies of severe pain/vaginal lesions, six reports of allergies, nine of urinary tract complaints (three with hydronephrosis), and five of toxic shock syndrome following MC-use, with one in a woman with an intra-uterine device (IUD). IUD-dislodgment was reported among 13 MC-users (8 case-reports, 5 in one study) between 1 week and 13 months of IUD-insertion. MC-retention requiring professional assistance was reported among forty-six cervical cup users and two vaginal cup users. We identified 199 brands of MCs, and availability in 99 countries with prices ranging from US$ 0.72-46.72 (median 23.3, 145 brands). The overall quality of studies was low.

**Interpretation**

Evidence indicates that MCs are a safe option for menstruation management and are being used internationally. The review was limited by the lack of high-quality studies.

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**Research in context**

**Evidence before this study**

A lack of affordable and effective menstrual products can result in leakage and chaffing in menstruating girls and women and can impact their health and education. There has been a recent increase in programmes to provide menstrual products to assist women and girls. The menstrual cup (MC), a receptacle used to collect blood flow has received limited attention. This in part may reflect concerns about insertable products as either culturally unacceptable or due to prior public health alerts such as toxic shock syndrome associated with highly absorbent tampons. Information about leakage, acceptability, and safety of MCs is needed to support organizations to make informed decisions and provide more comprehensive menstrual health education for girls and women. We searched PubMed, Cochrane library, Web of Science, Popline, Cinahl, Global Health database, Emerald, Science.gov, WorldWideScience and Google Scholar with the keywords “(Menstrual Cup) AND Review” on 24 November 2018 to determine if a review of MCs was available with information on leakage, acceptability, and safety. No review was identified, but a literature review by van Leeuwen and Torondel (2018) on menstrual management in emergency contexts noted a lack of empirical evidence examining the introduction and testing of MCs in humanitarian settings.

**Added value of this study**

To our knowledge, this is the first systematic review and meta-analysis examining girls and women’s experiences of MCs, aggregating outcomes from 43 studies and 3319 participants asked about their use or willingness to use MCs. We provide information on leakage compared to other products, a listing of known adverse events, other uses of the MC, and quantitative and qualitative information on acceptability in both high and low/middle income countries. Information is provided on availability and prices of MCs. Serious adverse events were not common, with five reported cases of toxic shock syndrome (TSS). However, the number of MC-users is unknown, so comparisons of TSS risk between users of tampons or the intravaginal diaphragm cannot be made. While MCs are manufactured and available globally they are not commonly mentioned in puberty education materials for girls.

**Implications of all the available evidence**

The available evidence suggests that MCs seem an effective and safe alternative to other menstrual products. Further research globally can provide more information on acceptability. Information on MCs should be provided in puberty education materials. Policy makers and programmes can consider this product as an option in menstrual health programmes. More research is needed to monitor adverse events and evaluate best practice to shorten the familiarisation phase required for safe and effective use, and on cost-effectiveness and environmental impact.

**Introduction**

Girls and women need effective, safe, and affordable menstrual products. Globally, an estimated 1.9 billion women – around 26% of the world population – were of menstruating age in 2017, spending on average 65 days in the year dealing with menstrual blood flow.1 Menstruation is a normal body function and a sign of reproductive health.2 Few solutions are available to manage menstruation; additionally, ignorance, prejudice, costs or safety fears can impede girls and women from testing the full range of products available. A lack of affordable and effective menstrual products can result in leakage and chaffing in menstruating girls and women and can impact their health.3,4 Use of poor-quality materials has been shown to predispose women to an increased risk of urogenital infections including bacterial vaginosis.5-7 In some situations, mostly researched in low- and middle-income countries (LMIC), menses can affect girls’ schooling,8 can make women and girls a target of sexual violence or coercion,9,10 and can affect employment and work experience of women.11,12 In LMIC, a lack of water, sanitation, and hygiene (WASH), inadequate education, and poor disposal facilities, raise public health concerns, particularly among schoolgirls.8,13 In high income countries (HIC) and LMIC, there is an increase in policy-led initiatives and donations to provide menstrual products, e.g. to keep girls in school. To allow such organisations to make informed decisions, information is needed on the range of menstrual products.

The menstrual cup (MC) is not commonly known, despite its long history (<https://en.wikipedia.org/wiki/Menstrual_cup>; appendix page 2).14 Like tampons, MCs are inserted into the vagina, but the blood is collected in the receptacle which can hold 10-38 ml of blood. MC emptying occurs 4-12 hours depending on menstrual flow and type of cup. Currently, there are two; a vaginal cup, which is generally bell-shaped and placed in the vagina, and a cervical cup which, like a diaphragm for contraception, is placed around the cervix high in the vagina. MCs are made of medical grade silicone, rubber, latex or elastomer and can last up to 10 years; disposable single-use MCs also exist.

We conducted a systematic review of the medical and grey literature to summarize current knowledge about leakage, safety, and acceptability of MCs and compared where available with other menstrual products. Information on global availability and costs of MCs were compiled, preliminary estimates on costs and waste savings were made, and guidance materials on menarche in selected regions of the world were examined for reference to MC as a product option.

**Methods**

*Search strategy and selection criteria*

This analysis complies with the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement (appendix 2). The protocol was registered in the International Prospective Register of Systematic Reviews (CRD42016047845). To be eligible for inclusion in the review, the material needed to have information on leakage, acceptability or safety of MCs. Quantitative, qualitative, or mixed design studies were included. Animal studies, and studies using MCs to collect vaginal fluids without participants’ reported experiences during menstruation were ineligible.

*Identification of studies*

The search only included material in English; keywords included “(Menstrual AND Cup) OR (Menses AND cup) OR (Menstruation AND Cup) OR (Vaginal AND Cup)”. The following databases were searched: PubMed, Cochrane library, Web of Science, Popline, Cinahl, Global Health database, Emerald, Google Scholar, Science.gov and WorldWideScience. Studies were eligible from the inception of the databases used; the last search was conducted on 14 May 2019. We screened the Manufacturer and User Facility Device Experience (MAUDE) database from the U.S. Food and Drug Administration for menstrual cup related events (10-year limit, last search 28 May 2019).15 For information on costs and availability, we screened websites of MC manufacturers using different web listings, and web searches and consulted experts.

*Data collection and study appraisal*

Study eligibility, data extraction and risk-of-bias assessment were performed independently by two reviewers (AMvE & ML for quantitative and LM & GZ for qualitative studies); differences were discussed until agreement was reached. The main outcome was menstrual blood leakage when using the MC. Information on acceptability of MC-use included difficulty with insertion or removal, comfort of wearing, and future use. Safety included serious adverse events, such as toxic shock syndrome (TSS), vaginal abrasions and effect on vaginal microflora (e.g. vaginal discharge, infections), effects on the reproductive, digestive or urinary tract, and safety in poor sanitary conditions. Other safety issues identified only during the review (e.g.*,* retention requiring clinical assistance) were documented, and all material was re-reviewed to ensure completeness of the safety assessment. The Cochrane tool for trials was used for quality assessment, and an adaptation of the Newcastle-Ottawa tool (appendix page 5) was used for observational studies.16,17 The Critical Appraisal Skills Programme tool was used to examine the quality of qualitative studies.18 For estimations on costs of disposable pads and tampons, we explored prices for commonly used products in six countries (USA, UK, India, Spain, China and Canada) and calculated average costs per product; extrapolating information on content and weight of menstrual products,19 we estimated waste and costs for a range of 9-25 units per product per month and compared these to consistent MC-use of one MC for 10 years. Additional information on methods used to assess MC information, availability and prices, qualitative studies, and costs and waste and additional information on data extraction are available in the appendix (page 3-5).

*Synthesis of quantitative and qualitative studies*

Results were tabulated as a narrative synthesis. If trials or studies presented sufficiently homogeneous data in terms of design, we pooled results (proportions) using meta-analyses and a random effects model (Metaprop, Stata version 14.2.2) with heterogeneity quantified using the *I*² statistic (appendix page 3). We integrated the quantitative and qualitative analyses for the acceptability of MC-use. Sensitivity analysis was performed using the quality assessment (low versus moderate-to-good quality study). We used two-tailed p-values of <0.05 to indicate statistical significance.

**Role of the funding source**

The funders had no role in study design, data collection, data analysis, data-interpretation or writing of the report. The corresponding author had full access to all of the data and had final responsibility to submit for publication.

**Results**

***Characteristics***

Of 436 unique records identified (appendix page 6), 59 were relevant (figure 1), and 43 studies were eligible (table 1), comprising 3319 participants who used or were asked about the MC.6,14,15,20-74 Seven studies were among schoolgirls in LMIC (647 participants or 19·5%).6,28,33,44,54,57 Three studies were conducted in the early 1960s, six in the late 1980s, and most in the past decade (26); 15 were from LMICs. Most studies reported on vaginal cups (63%) and were journal articles (81.4%). At least seven described MCs that are no longer available (Tassette, Tassaway and Gynaeseal). The quality of quantitative studies was low, with only three of moderate-to-high quality (table 1; appendix page 7-8). Observational studies were not clear on the source of participants, or participants were not representative of the community. Six studies, all from LMICs, provided qualitative information (appendix page 10).

***MC and leakage***

Only four studies made direct comparisons between MCs and usual products; the outcomes examined were different, but leakage was similar in three and significantly less among MCs for one study (figure 2).24 In studies using MCs which are still marketed, the proportion of leakage ranged from 2-31% for a wide range of definitions. Some factors mentioned in association with leakage by study authors included menorrhagia,47 unusual anatomy of the uterus,51 need of a larger MC size,6 and incorrect MC placement or filled to capacity.38,51

***Adverse events and side-effects***

MC-use was not associated with abnormalities in the vagina or cervix in three studies with vaginal examinations (n=370, table 2).14,50,65 Three MC-users reported vaginal wounds in case-reports, which could not be confirmed with medical records. There was one case-report (self-report) on pain on removal and one on pain when wearing the MC (self-report),15 and two reports from cohort-studies on vaginal or cervical irritation without clinical consequences.38,42 Three adverse events from cohort-studies and three case-reports were possibly related to an allergy; one case of silicone allergy necessitating reconstructive vaginal surgery was reported.14,15,47 Difficulty with removal requiring professional assistance was reported 47 times for cervical cups and twice for vaginal cups (one from cohort-study and 46 case-reports).14,15,45,60

There was no increased infection risk (reproductive tract or systemic infection) associated with MC-use among European,52,53 North American, and African women and girls,6,20 compared with other menstrual products. A decrease in *candidiasis* was reported with MC-use in two of four studies; one found no candidiasis infections at follow up (0/18, 0.0%) and the other, a randomised feasibility pilot among school girls in Kenya comparing MCs, sanitary pads and usual practice (cloth, pads, tissue, or other makeshift materials), showed no difference in *candidiasis* by study arm (MC: 11/144, pads: 19/200, usual item 13/156, p=0.68 and 0.87 for MC vs. pads and MC vs. usual item, respectively).6,14,55,65 One study reported lower infections rates among MC-users compared to tampons or pads (not further specified), and a randomized pilot study in Kenya reported lower bacterial vaginosis among MC-users enrolled for ≥9 months (MC: 13/101, pads: 29/143, usual item 20/104, p=0.018 and 0.074 for MC vs. pads and MC vs. usual item, respectively).6,65 TSS was identified in five case-reports;14,15,62 microbiological confirmation was available with cultures from MC and blood showing streptococcus for one case. In two cases, concomitant conditions were present (intra-uterine device [IUD] in situ; an immunodeficiency disease).15,62 The prevalence of vaginal *Staphylococcus aureus* was examined among Kenyan schoolgirls participating in a randomized pilot study; no difference was seen between MC, pads and ‘usual practice’ arms.30 No toxic shock syndrome toxin (TSST-1) was found expressed in *S. aureus* positive samples of MC-users30 In-vitro studies of TSST-1 production in the presence of MC-material showed conflicting results.66,67

In a MC-IUD case-report and a case series (7 women), dislodgements of an IUD during removal of the MC were described between 1 week and 13 months of IUD insertion;15,73 a retrospective chart survey did not find an increased risk for IUD expulsion within 6-8 weeks after insertion among MC-users (5/135, 3.7%), compared to users of tampons (11/469, 2.4%) or pads (7/169, 4.1%).56

One case-report suggested MC-use may have been associated with the development of endometriosis;64 however, this was not considered plausible by the regulatory authority and no further reports were published on this possible association. There were three case-reports of hydronephrosis and one of incontinence when using the MC; symptoms disappeared after MC removal.15,58,59 (For other uses of MCs, see appendix page 9.)

***Menstrual cup uptake and acceptability: qualitative and quantitative analyses***

All six qualitative studies were from LMIC (appendix page 10-13),31,33,34,54,55,57,75 while studies with quantitative information on uptake and acceptability were from both LMIC and HIC (appendix page 14-22).14,20,23-25,33,38,42-45,47-52,55,68,75 In LMIC, usual products for menstruation included cloths, disposable pads, cotton wool, tissue paper or other items; leakage and chaffing is a common concern.31,33,34,54,76 All studies involved used some form of education and training on the MC. Girls and women expressed initial concerns in qualitative studies, noting the size of the MC.31 Many were concerned it could cause pain (and noted it often did so at first) or worried about reproductive harms (e.g. infertility). In quantitative studies, three percent (pooled estimate) of participants reported they could not insert the MC (95% CI 1-6%, 11 studies, *I2* 79·3%, 1251 women) and 11% (3-27%, 10 studies, *I2* 96·4%, 1190 women) reported MC-related discontinuation (table 3). Pain on insertion was reported among 10/106 (9·4%) for MC-use versus 0/104 (0·0%) when continuing their usual method at 3 months follow-up in a South African cross-over trial (p-value not reported).20 Initial discomfort on insertion was reported by 20% of participants (pooled estimate, 95% CI 12-30%, 17 studies, *I2* 92·3%, 1061 women, appendix page 20). All qualitative studies described user-familiarisation with the MC over time, with practice, peer support and training key to success.31,33,34,54,57,75 Longitudinal quantitative studies in LMIC demonstrated a learning curve of 2-5 months (appendix page 22); use of MC-colour-change as an objective measure suggested usage increased throughout the first year among Kenyan school-girls.68 The Nepalese study noted that self-reported increased usage two months after distribution was associated with the presence of friends who successfully used the MC.26 In India and Tanzania, the uptake of MCs was significantly slower than pads (appendix page 24).23,44 In 15 studies with information, 73% (59-84%, pooled estimate, *I2*96%, 1144 women) reported willingness to continue MC-use after the study (figure 3). All qualitative and some quantitative studies reported a positive effect of MC-use on participants’ lives, reduced stress concerning staining and leakage, and improvements in mobility.14,49,51 Challenges described included difficulties with MC cleaning and storage in LMIC.34,54 Other challenges related to emptying the MC in school or public toilets,29,34,54 which was also reported by HIC-participants.37 MCs were associated with a reduction in average number of changes per cycle in a UK study compared to tampons or sanitary pads.52 Three qualitative studies implied that school attendance, concentration and performance improved after participants received a MC.31,34,54 No measured difference in school absence or test results between products were reported (appendix page 24).6,28,34 A study in Nepal noted a significant reduction in time spent doing laundry when comparing MC-users to users of product-as-usual.28 The economic advantage of an MC emerged in qualitative studies, with participants (and families) citing monthly cost-savings from not needing to purchase pads or soap for washing cloths. Two qualitative studies included participant quotes illustrating that MCs may reduce the need for transactional sex to purchase pads.34,75 This may be corroborated by the results from a randomised controlled study among schoolgirls which noted a significantly lower prevalence of sexually transmitted infections among participants who were provided by the study with either MCs or disposable pads versus controls (using usual products), citing lower exposure to transactional sex as a likely reason (table 2; appendix page 24).6 There was considerable heterogeneity in the pooled meta-analyses (*I2*≥74%, table 3).

**Use of menstrual cups in challenging sanitary conditions**

A study among school girls in Kenya in an area with poor WASH77 reported on dropping of menstrual products during changing/emptying.32 The frequency was similar for MCs and sanitary pads. Factors involved included young age, lack of time, and privacy; MC-dropping decreased with increasing experience (approximately 23% in the first three months and 10% in 12+ months).  This was associated with *E. coli* isolated in cultures from MC swabs, which was higher in new users compared to experienced users (table 2).30 A verbal report of handwashing before MC-change was 95% in Kenya, 70% in Uganda, and 94% in a refugee camp.29,55,75 When facing a lack of water in toilets, some participants reported carrying a bottle of water for when they emptied their MC.29 Others said they had to empty the MC only twice a day, so they could avoid emptying in public places.75 In two studies, women reported that MCs saved water, because there was less leaking and washing of cloths.33,75  Privacy was mainly mentioned as a problem when boiling or storing MCs.55,75

***Visibility, availability, costs and waste***

In three studies in HIC, only 11-33% of the women interviewed (n=375) were aware about MCs (appendix page 25).37,46,53 In 69 websites with educational materials on menarche from 27 countries, disposable pads, tampons, MCs, and reusable pads were mentioned by 76·8%, 65·2%, 30.4% and 21.7%, respectively (appendix page 26-28). We identified 199 brands of MCs, and availability in 99 countries with prices ranging from US$ 0.72-46.72 (median 23.3, 145 brands) (appendix page 29-34). Using accumulated estimates over 10 years, purchase costs and waste from consistent MC-use (vaginal cup) would be a small fraction of the purchase costs and waste of pads or tampons: e.g. if compared to using 12 pads or tampons per period, MC-use would comprise 5% and 7% of the purchase costs and 0·4% and 6% of the plastic waste respectively (appendix page 35-37).

**Discussion**

Women, girls and transgender people require hygienic menstrual products monthly to lead healthy and productive lives. In this review we evaluate the MC, combining information from medical and grey literature to inform choice and strengthen the evidence-base for programmes supporting menstrual health, such as for schoolgirls in LMIC or among refugees. Leakage was similar or less when using the MC compared with disposable pads and tampons. The adoption of MC required a familiarisation phase and peer support seemed important for their uptake in LMIC; challenges in resource constrained settings (lack of sanitation, hygiene and privacy) did not stop women from using them, and advantages were reported. Around 70% of participants in 13 studies declared wanting to continue use. There were incidental case-reports on vaginal damage or toxic shock syndrome or urinary tract complaints following MC-use, and difficulty in retrieving the MC can occur. MC-use has been described as a factor for IUD dislodgement. MCs were infrequently mentioned in puberty education for adolescent girls; the lack of information appears global. Brands of MCs were identified in over 70 countries with a wide range in prices averaging US$ 22·90.

In studies which examined the vagina and cervix during follow up, no mechanical harm was evident from MC-use.14,50,65 There did not seem to be an increased infection risk, and, compared to pads and tampons, some studies indicated a decreased infection risk.6,14,65 The study in Kenya that detected lower bacterial vaginosis compared with sanitary pads, postulated that the inert material of MCs may assist in maintaining a healthy vaginal pH and microbiome.6 Reported pain may relate to variations in the pelvic anatomy or wrong positioning of the MC leading to internal pressure. This could account for case-reports of hydronephrosis or urinary incontinence. Allergies to the materials used in MCs are not common, but women should be aware of the possibility and keep this in mind when starting use; however, it may be difficult for women who start MC-use to discriminate between discomfort as part of the normal learning curve or pathology. Laboratory studies have shown contradicting results on the possibility of TSST-1 development in the presence of MCs but clinical data in humans using cups have so far not shown reason for concern. The reported risk of TSS with MC-use seems low, with five cases in the literature. While aggregated data on the number of MCs sold or used is unavailable, we anticipate the number of girls and women using 199 different brands globally is likely to be thousands. In the USA, the rate of all types of TSS was around 0·8-3·4 per 100,000 population, while menstrual TSS was reported in 6-12 per 100,000 users of high absorbency tampons in 1980. Similarly, among women using female barrier methods, which also uses medical grade silicone or latex products, TSS is low (~2·25 cases per 100 000 users per year).78

The combination of IUD and MC-use may need further study, given the growing number of case- reports of dislodging of IUD following MC removal; it is possible that IUD-users may need to consider alternative options for either family planning or menstrual flow. Given the limited number of case-reports and studies thus far, we cannot yet exclude other issues with MC-use. There were only a limited number of studies which directly compared MCs and usual methods for leakage; however, current data do not suggest the MC is less effective than other sanitary products. MCs can collect more blood than tampons or sanitary pads and have been adopted by women with menorrhagia.49 The studies reviewed report that under challenging conditions e.g. with limited water supply or privacy, MCs can be used. Alternatives to MCs and disposable sanitary pads include reusable pads, so far evaluated in few studies.79-82 In Uganda, privacy to dry these pads was a challenge, suggesting additional packs would be needed to ensure effective laundering.83

*Limitations*

We used leakage as a primary outcome in this review; however, the outcomes identified in the reports reviewed varied by different time points and designs, prohibiting combination of results when directly comparing MCs versus “other item”. The quality of studies was a limitation, with only two assessed to be of good quality and this will potentially have contributed to bias in the meta-analyses. Part of the information was from older studies when reporting requirements were less stringent or with MCs that are not available anymore, from reports not published in peer-reviewed journals, and from studies using the MC to evaluate other topics. Recruitment for observational studies was not representative or clear. Studies mostly depended on self-reporting, which may have overestimated MC-use. One study comparing self-reporting against a conservative but objective measure of MC-colour-change found MC-use was slower, e.g. by 4 months 75% of recipients stated they had started using it, whereas only by 10 months, 75% of MCs showed cup-colour change.68 Denominators on total MC-users were unavailable as brands guard consumer marketing data. Countries where MCs were available may be underestimated because MC-producers in LMIC may not always have websites. Our search was in English, and thus lacked information from many countries e.g. Russia or China.  The heterogeneity was high in the pooled meta-analyses (*I2*≥74%, table 3), indicating there is inconsistency in findings across studies. Given the high variability in study design and period, study population, and products examined, this might not be unexpected.It is unknown what proportion of adverse events are under-reported; we did not identify many (one case of TSS) when exploring the internet (appendix page 38-39). The MAUDE database only allows web searches for the previous 10 years. Our cost and waste estimates are illustrative and do not take into account the combined use of menstrual products during a period (e.g. panty liners for light days), or inflation and production costs.

*Conclusion*

This review of international experiences shows MCs can be an acceptable and safe option for menstrual hygiene in HIC and LMIC but are not well known and can inform policy makers and programmes that MCs can be an alternative to disposable sanitary products, even where water and sanitation facilities are poor. However, provision of information and training and follow-up on correct use may be needed. Further studies are needed on cost-effectiveness and environmental impact comparing menstrual products, and to examine facilitators of MC-use, with monitoring systems in place to document any adverse outcomes.

**Contributors:** AMvE & PAPH led the conception and design of the study. AMve, GZ, ML & LM led the development of the data collection instrument, data collection and quality assessment. AMvE, GZ, ML, & LM conducted the statistical analysis, interpreted the data, and wrote and revised the manuscript. MS, EN, HU, & KL contributed to study design, assisted in data interpretation, and revised the manuscript. All authors contributed to data interpretation and revised the intellectual content of the manuscript.

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**Declaration of interests**:AMvE, GZ, ML, LM, MS, EN, HU, KL and PAPH declare no competing interests.

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***Table 1:*** **Characteristics of studies contributing to Menstrual Cup review**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Studies**  | **Material** | **Location** | **Time** | **Design** | **Sample size and population** | **Age (years) & menstrual flow as defined by source** | **Menstrual cup brand\* (type)** | **Comparison (if trial)** | **Follow up (fup)**  | **Outcomes** | **Loss to fup (%)** | **Quality score** |
|  |  | **TRIALS** |
| Beksinska 201520-22 | Journal article | Durban, South Africa, 2013 | 2013 | Individually randomized cross-over trial | 110 women | Mean 29, sd 6, range 18-45. Heavy flow: 46.2% | Mpower Mcup(vaginal) | Usual product (disposable pads, tampons, cloths) | 6 cycles (3 cycles each product) | Acceptability Performance | 4.5 | 5 |
| Hoffman 201423 | Journal article | Jehanabad district, Bihar, India | 2012 | Cluster-randomized trial | 960 women, (174 in MC arm and 46 MC by choice) | Mean 29·9, sd 6·7. No information on heavy flow | Not reported | Usual product(Cloth & disposable pads) | 8 months | Acceptability, demand for high-barrier menstrual cup and low-barrier sanitary pads | 15.8 (6 mo) | 4 |
| Howard 201124 | Journal article | Vancouver, Canada | 2006-2007 | Individually randomized  | 110 women (56 in cup arm)  | Range 19-40. Heavy flow: 11.1%  | Divacup (vaginal) | Tampons | 4 cycles | Use, use in future, costs and waste | 11.8 | 3 |
| Oster 201125Oster 201226Oster 200927,28 | Journal article | Bharatpur, Chitwan district, Nepal | 2006-2008 | Individually randomized trial | 199 school girls (98 in cup arm) | Mean 14·2, sd 1·2. No information on heavy flow | Mooncup (vaginal) | Usual product(Cloths & disposable pads) | 15 months | School attendance, peer effect | 0.5 | 3 |
| Phillips-Howard 20166Nyotach 201529Juma 201730Mason 201531Oduor 201532van Eijk 201868 | Journal article | Gem district, Siaya Province Kenya | 2012-2013 | Cluster randomized trial | 766 school girls (229 in cup arm)  | Mean 14·6, sd 0·7. Heavy flow: 20.8% | Mooncup (vaginal) | Disposable pads and “usual practice” (cloths and pads) | median 10·9 months | School drop-out, STIs, reproductive tract infections | 15.7 | 6 |
|  |  | **OBSERVATIONAL STUDIES** |
| **Studies** | **Material** | **Location** | **Time** | **Design** | **Sample size and population** | **Age (years) & menstrual flow**  | **Menstrual cup brand (type)** | **Usual practice before cup** | **Follow up** | **Outcomes** | **Loss to fup (%)** | **Quality score** |
| APHRC 201033-35 | Report | Nairobi, Kenya | 2008 | Cohort | 36 women, 60 school girls | NR. No information on heavy flow | Mooncup (vaginal) | Disposable pads, cloths, cotton wool, tampons | 3 cycles | Feasibility | 6.3 | 2 |
| Averbach 200936 | Journal article | Epworth, Zimbabwe | 2007-2008 | Survey & FGD | 43 adult women | Range 18-45 | Duet (cervical, re-usable) | Cotton wool, cloths, disposable pads, tissue | NA | Consideration of MC- use | NA | ND |
| Borowski 201137 | Master Thesis | USA | 2011 | Survey | 155 women  | 5 18-24 years, 69 25-34, 49 35-44, 36 45+ years | No particular brand | NR | NA | Consideration of eco-friendly menstrual products | NA | ND |
| Care International Uganda 201875 | Report | Refugee Settlement, Uganda | 2018 | Cohort | 80 girls and women and 20 female trainers | 15-30 years, 25 ≤18 years. No information on heavy flow | Ruby cup  | Disposable and reusable pads, cloths | 3 months | MC-use | 53.8 | 2 |
| Cattanach 199138Cattanach 199040† | Journal article | Hawthorn, Australia | NR | Cohort | 80 women, out of 259 approached | Range 17-42. No information on heavy flow.  | Gynaeseal (cervical) | NR | 18 months | Acceptability | 69.1 | 2 |
| Cheng 199542 | Journal article | NR, Canada | 1991-1992 | Cohort | 51 women | 46/51 <40 years (90·2%). Moderate to heavy flow: 42/51 (82.4%) | Menses cup‡ (vaginal) | Tampons and disposable pads | 2-13 cycles | Acceptability of MC for measuring flow | NR | 2 |
| Chintan 201743 | Journal article | India (several sites) | NR | Cohort | 100 women | Range 14-55. No information on heavy flow | Flow care (vaginal) | Disposable pads and tampons | 8 weeks | MC-use | NR | 2 |
| Femme International 201744 § | Report | Kilamanjaro regionTanzania  | 2016-2017 | Cohort | 184 adolescents, 38 women | Range 12-54. No information on heavy flow | Ruby cup (vaginal) | NR | 6-12 months | MC-use | 37-88 | 2 |
| Ganyaglo 201970Ryan 201871 | Journal article & abstract | Ghana | 2016 | With/without trial | 11 adult women | Mean 43.6, sd 12.3. MC-use for fistula | Diva cup | Pads | 4 hours | MC-use for vesicovaginal fistula | 0 | 5 |
| Gleeson 199345 | Journal article | Dublin, Ireland | NR | Cohort | 22 women | NR. 12 (54.5%) women with menorrhagia | Gynaeseal (cervical) | Tampons | 1 cycle | Leakage, ease, use for measuring flow | 0 | 3 |
| Grose 201446 | Journal article | California, USA | NR | Survey | 151 under-graduates | Range 18-23.  | Brand not reported | NR | NA | Consideration of menstrual cup | NA | ND |
| Kakani 201747 | Journal article | Dharpur, Gujarat, India | NR | Cohort | 158 women | Mean 31, sd 6·1, range 21-50. Heavy flow: 20/150 (13.3) | NR: 44 mm diameter, thin walled silicon ‖ | Cloths, disposable pads, tampons | 3 cycles | Acceptability and efficacy | 5.1 | 3 |
| Madziyire 201848,69 § | Journal article | Epworth, Zimbabwe | 2016-2017 | Cohort | 54 women | Range 18-45. No information on heavy flow. | Butterfly (vaginal) | NR | 3 cycles1 year | Acceptability, leakage | 3.7 | 3 |
| North 201114 | Journal article | USA (7 centres) | NR | Cohort | 406 women | Range 18-55. No information on heavy flow. | Soft cup¶ (disposable cervical) | Disposable pads and/or tampons | 3 cycles | Safety, effectiveness and acceptability | 24.1 | 3 |
| Parker 196649 | Journal article | Ann Arbor, USA | NR | Cohort | 46 women with menorrhagia, 19 with normal flow | NR. 46 women with menorrhagia, 19 with normal flow | Tassette (vaginal) | Tampons and disposable pads | 2-6 months | Acceptability | 15.2 | 3 |
| Pena 196250 | Journal article | Florida, USA | NR | Cohort | 125 women (100 with normal flow and 25 with vaginal infections) | Range 20-45. All “Normal flow” | Tassette (vaginal) | Tampons and disposable pads | 3 cycles | Not clear | NR | 2 |
| Shihata 201451 | Journal article | Sweden, USA, Mexico, Brazil, Colombia | 2013 | Cohort | 146 women | Range 18-40. No information on heavy flow. | FemmyCycle (One size, vaginal) \*\* | Disposable pads, tampons | 3 cycles | Leakage, acceptability | 28.1 | 2 |
| Stewart 201052 | Journal article | Nottingham, UK | 2008-2009 | Cohort | 54 women | Mean 22·5, sd NR. No information on heavy flow. | Mooncup (vaginal) | Tampons and disposable pads | 6 cycles (3 with cup) | Leakage, acceptability | 61.1 | 2 |
| Stewart 200953 | Journal article | Nottingham, UK | NR | Survey | 69 clinic patients | 18 <30, 21 30-40, 30 40+ yrs. No information on heavy flow.  | Mooncup (vaginal) | Tampons and disposable pads | NA | Consideration of MC | NA | ND |
| Tellier 201255 | Report | Kitgum, Uganda | NR | Cohort | 31 women | Mean 24, sd NR. No information on heavy flow.  | Ruby cup (vaginal) | Cloths, gauze, disposable pads | 3-5 cycles | Acceptability, safety | 51.6 | 3 |
| Wiebe 201256 | Journal article | Vancouver, Canada | 2009 | Retrospective chart survey | 930 women, 96 used MCs | 59% <30 years. No information on heavy flow.  | No particular brand or type | NA | 6 weeks | IUD expulsion within 6 weeks after placement by menstrual product used | NA | ND |
|  |  | **STUDIES WITH ONLY QUALITATIVE INFORMATION** |
| **Studies** | **Material** | **Location** | **Time** | **Design** | **Sample size and population** | **Age (years) & menstrual flow** | **Menstrual cup brand (type)** | **Follow up (fup)** | **Outcomes** |  | **Quality score** |
| Hyttel 201754 | Journal article | Bungatira, Gulu, Uganda | 2013 | 2 focus group discussions & 6 semi-structured interviews | 36 school girls (purposely selected) | Mean 14·6, sd 0·7, range 13-17 | Ruby Cup (vaginal) |  | 3 cycles | Willingness and ability to use †† | NA  | Medium |
| Sundqvist 201557 | Thesis | Msiriwa, Tanzania | 2014 | In-depth interviews | 15 school girls | 14-15 | Lady cup (vaginal) |  | NR | Effect of menstrual cup use on education and social interactions | NA  | Strong |
|  |  | **CASE REPORTS** |
| **Studies** | **Material** | **Location** | **Time** | **Design** | **Sample size and population** | **Information age participants** | **Menstrual cup brand (type)** | **Follow up (fup)** | **Outcomes** |  | **Quality score** |
| Adedokun 201758 | abstract | Brno, Czech Republic | NR | Case Report | 1 adult woman | 30 | NR | NR | Hydronephrosis | NA  | ND |
| Nunes-Carneiro 201859 | Journal article | Porto, Portugal | NR | Case Report | 1 adult woman | 26 | NR | 5 days | Uretero-hydronephrosis | NA  | ND |
| Stolz 201972 | Journal article | France or Switzerland | NR | Case Report | 1 adult woman | 47 | NR | “couple of weeks” | Hydronephrosis | NA  | ND |
| Day 201260 | Journal article | London, UK | NR | Case Report | 1 adult woman | 20 | Mooncup (vaginal) | NR | MC retention | NA  | ND |
| U. S. FDA Maude database15 | Results database search | USA | 1950-June 2018 | Case reports | 12 women | NR | Mooncup, Diva cup, Femmy cycle, Softcup (vaginal and cervical) | Variable | See adverse events table | NA  | ND |
| Seale 201973 | Journal article | USA | NR | Case Series | 7 women | 16 years: 1, 22-25 years: 6 | NR | 2-12 months | IUD expulsion | NA  | ND |
| Goldberg 201661 | Journal article | New Brunswick, Canada | 2013 | Case Report | 1 adult woman | 39 | NR (vaginal) | NR | Use as diagnostic aid of vesicouterine fistula | NA  | ND |
| Mitchell 201562 | Journal article | Ontario, Canada | NR | Case Report | 1 adult woman | 37 | DivaCup (vaginal) | Two weeks post-admission | Possible Toxic Shock Syndrome | NA  | ND |
| Russell 201663 | Journal article | Utah, USA | NR | Case Reports | 3 adult women | 54, 60 and 68 | NR (vaginal) | NR | Use as enterovaginal or vesicovaginal fistula control | NA  | ND |
| Spechler 200364 | Journal article | Bethesda, USA | NR | Case Report | 1 adult woman | 41 | Keeper (vaginal) | 2 years post- surgery | Adenomyosis and endometriosis | NA  | ND |
|  |  | **OTHER TYPE OF STUDIES WITH RELEVANT INFORMATION**  |
| **Studies** | **Material** | **Location** | **Time** | **Design** | **Sample size and population** | **Age (years)** | **Menstrual cup brand (type)** | **Follow up (fup)** | **Outcomes** |  | **Quality score** |
| Cattanach 198939† | Journal article | Hawthorn, Australia | 1986-1988 | Vaginal samples | 5 women | Range 19-32 | Gynaeseal\* (cervical) | 3-22 months | MC safety: Effect on vaginal flora | NA  | ND |
| Karnaky 196265 | Journal article | USA | NR | Vaginal observations and samples | variable (20, 50 & 97 women) | NR | Tassette (vaginal) | 1 time- point | MC safety: Effects on vagina | NA  | ND |
| Tierno 198974 | Journal article | New York, USA | NR | In-vitro study | 16 menstrual cups | NA | NR | NA | Ability to induce TSST-1 production by TSS-associated strains of Staphylococcus aureus | NA  | ND |
| Tierno 199466  | Journal article | New York, USA | NR | in-vitro study | 6 menstrual cups | NA | Tassaway (vaginal) | NA | Ability to induce TSS toxin-1 by a TSS strain of Staphylococcus aureus MN8 | NA  | ND |
| Nonfoux 201867 | Journal article | France | NR | in-vitro study | 4 menstrual cups | NA | 2 be’Cup® and 2 MeLuna® (vaginal) | NA | Effect on Staphylococcusaureus growth and TSST-1 production using the modified sac method  | NA | ND |

Abbreviations: IUD=intra-uterine device. Fu=follow-up. MC=menstrual cup. Mo=month. NA=not applicable. ND=Not done (these studies were not assessed for quality). NR= not reported. Sd=standard deviation. STIs=sexually transmitted infections. TSS=Toxic shock syndrome. TSST-1=toxic shock syndrome toxin 1. Cloths=pieces of material (clothing, blankets, socks) which are used for menstruation and can be reused after washing or disposed of after use.

\*For manufacturing company, city, country and website where available, see table S4 in the appendix (page 7).

† Gynaeseal: disposable cup covering the cervix. This type of cup can also be worn during intercourse. The study author was the developer of Gynaeseal. We assumed the articles from 1990 and 1991 described the same study and used the publication with the larger sample size (1991).

‡ From Shanghai Newasia Medical Rubber Factory, Shanghai, China. This type of cup has a drainage tube that can be opened to let menstrual fluids pass.

§ Additional information obtained from internal report or author.

‖ Description in article is like a cervix-covering cup (“The device- the menstrual cup we utilized for the study is an internally worn device with a pliable rim 44mm in diameter and a thin-walled reservoir to collect and hold the menstrual fluid. It was designed to minimize bulk in order to facilitate insertion and removal. Once inserted; it opens to an oval shape, positioned between the posterior fornix and the notch behind the pubic bone, covering the cervix. Removal is accomplished by hooking a finger over the rim behind the pubic bone. It is made up of health grade non-toxic non- allergic silicon”), but image is of a low vaginal cup.

¶ Instead Softcup (Instead, Inc., San Diego, CA): disposable cup covering the cervix. This type of cup can also be worn during intercourse.

\*\* Author has patent on this menstrual cup.80

†† Part of a larger study (Gulu Schoolgirl Menstrual Cup Study, n=194) for which no other publication could be retrieved.

***Table 2:* Safety and side effects of the menstrual cup**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Issue** | **Menstrual Cup (type)** | **Numbers (%) or description** | **Notes** | **Source** |
| **Handling and positioning of menstrual cup** |  |
| Vaginal wound | Cup not clear (Divacup or softcup?) | Event April 2012. Vaginal wound experienced due to use of menstrual cup, needing treatment for vaginal bleeding from physician.  | Complete medical records were not available for evaluation | FDA Database15 |
| Softcup (cervical) | Reported April 2012. Long term customer of softcup product claimed vaginal scarring due to use.  | Medical director did not find anything in medical records provided by consumer related to vaginal health. | FDA Database15 |
| Softcup (cervical) | FDA database case report  | “…cup wore through the vaginal wall, damaging an artery that required surgical repair.” Could not be confirmed; no medical records available | North and Oldham 201114 |
| Vaginal pain on removal | Divacup (vaginal) | Event March 2017. Extreme pain on removal (first use). Person stopped using the cup.  | Self-report. No medical report available. | FDA Database15 |
| Pelvic pain | Softcup (cervical) | Event February 2017: pain lower pelvis, rectum and nausea about one hour after insertion, disappearing ~30 minutes after removal.  | Self-report. No medical evaluation available. Person stopped after trying twice. (Vascular compression?) | FDA Database15 |
| Vaginal irritation | Gynaeseal (cervical) | 1/73 (1·4%) | Self-report by participant | Cattanach 199138 |
| Cervix irritation | Menses cup (vaginal) | 1/51 (2·0%) | Pap smear normal | Cheng 199542 |
| Allergy and rash | NR, vaginal cup | Allergy: 1/150 (0·7%), rash: 2/150 (1·3%)  |  | Kakani and Bhatt 201747 |
| Softcup (cervical) | FDA data base: 2 case reports  |  | North and Oldham 201114 |
| Mooncup (vaginal) | Event in 2010: silicone allergy.  | Surgery was needed for vaginal repair.Manufacturer: Silicone allergy is very rare. | FDA Database15 |
| Difficulty with removal requiring professional assistance | Gynaeseal (cervical) | 1/22 (4·5%) |  | Gleeson 199345 |
| Softcup (cervical) | FDA data base: 3 case reports reported by North and Oldham 2011,14 1 event in 2018 |  | North and Oldham 201114, FDA Database15 |
| Softcup (cervical) | Reported complaints to company 2003-2008: Physician assisted removal 42  | Other complaints reported to company: poor fit 102, leakage 168, messy 98 | North and Oldham 201114 |
| Mooncup (vaginal) | Case-report: MC lodged on cervix, difficult to remove. | Moderate cervical inflammation after retrieval | Day 201260 |
| Divacup (vaginal) | Event April 2015: 1 case-report leading to emergency room visit |  | FDA Database15 |
| **Reproductive tract observations with menstrual cup use** |  |
| Vulva abnormalities | Softcup (cervical) | Baseline: 4/393 (1·0%), cycle 1: 8/365 (2·2%), cycle 2: 6/326 (1·8%), cycle 3: 5/305 (1·6%)  | Vulva-vaginal inspection at baseline and monthly for 3 months. No p-values reported | North and Oldham 201114 |
| Abnormalities of vaginal wall | Softcup (cervical) | 0/44 (0·0%)  | Vulva-vaginal inspection at baseline and monthly for 3 months | North and Oldham 201114 |
| Tassette (vaginal) | 0/12 (0·0%) | Vaginal inspection after 3 months | Pena 196250 |
| Tassette (vaginal) | 0/50 (0·0%) | Vaginal inspection conducted: timing of inspection not clear | Karnaky 196265 |
| Abnormalities cervix | Softcup (cervical) | Baseline: 23/390 (5·9%), cycle 1: 10/345 (2·9%), cycle 2: 6/326 (1·8%), cycle 3: 4/300 (1·3%)  | Inspection of cervix. No p-values reported for differences | North and Oldham 201114 |
| Softcup (cervical) | Abnormal pap test: baseline: 1/406 (0·2%), cycle 1: 1/368 (0·3%), cycle 2: 2/329 (0·6%), cycle 3: 0/308 (0·0) | Abnormal Pap test results were exclusion criteria at admission, and a reason for discontinuation of the study. No p-values reported for differences | North and Oldham 201114 |
| Condition of vaginal and cervical epithelium | Softcup (cervical) | “The Softcup caused no alteration or disruptionin vaginal or cervical epithelium, as assessed by colposcopy and cervical cytology” | 44 women examined at baseline, 37 at 2-3 months, and 25 at 5-6 months | North and Oldham 201114 |
| **Vaginal flora and infections with menstrual cup use** |  |
| Ph changes of vagina | Tassette (vaginal) | 0/50 (0·0%) | No abnormalities: vaginal areas where menstrual cup was placed were more acid66 | Karnaky 196265 |
| Softcup (cervical) | Mean pH: baseline 4·6 (n=400), cycle 1 4·6 (n=368), cycle 2 4·6 (n=329), cycle 3 4·5 (n=308) | No p-values reported | North and Oldham 201114 |
| Clue cells (vaginal smear) | Softcup (cervical) | Baseline: 6, cycle 1: 6, cycle 2: 5, cycle 3: 4 | Sample sizes not reported. No significant changes according to authors | North and Oldham 201114 |
| Lactobaccilus | Softcup (cervical) | “…before, during, and after use of the cup, vaginal Lactobacillus (normal vaginal flora) was maintained at normal levels.” | Data in Figure 3 in publication, can’t be extracted. No significant changes according to authors | North and Oldham 201114 |
| *Gardnerella vaginalis* | Softcup (cervical) | According to authors, no significant changes from baseline-cycle 3 | Data in Figure 3 in publication, can’t be extracted. | North and Oldham 201114 |
| Bacterial vaginosis  | Softcup (cervical) | According to authors, no significant changes from baseline-cycle 3 | Data in Figure 3 in publication, can’t be extracted. | North and Oldham 201114 |
| Mooncup (vaginal) | Endline survey: cups 21/144 (14·6%), pads 40/202 (19·8%) and usual item (control) 32/156 (20·5%), cups vs. control: p=0·11, cup vs. pads p=0.13. Among girls enrolled for ≥9 months: cup 13/101 (12·9%), pads 29/143 (20·3%), usual item 20/104 (19·2%); cups vs. control: p=0·07, cup vs. pads p=0.018 (p-values from source article) | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months. | Phillips-Howard 20166 |
| Candidiasis | Softcup (cervical) | Baseline: 6, cycle 1: 6, cycle 2: 3, cycle 3: 6 | Sample sizes not reported. According to the authors there was a significant decrease in yeast from month 1 to 2. | North and Oldham 201114 |
| Ruby cup (vaginal) | 0/18 vaginal candidiasis at follow up (3-5 months) |  | Tellier 201255 |
| Tassette (vaginal) | *C. albicans* decreased with the use of the cup | Data not reported | Karnaky 196265 |
| Mooncup (vaginal) | Endline survey: cups 11/143 (7·7%), pads 19/200 (9·5%), usual item (control) 13/156 (8·8%). MC vs. control: p=0·87, MC vs. pads p=0.68, p-values from source article | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months. | Phillips-Howard 20166 |
| Group B *Streptococcus* | Softcup (cervical) | No differences between baseline and cycle 1-cycle 3 | Data in Figure 3 in publication, can’t be extracted. No significant changes according to authors | North and Oldham 201114 |
| *Enterococcus* | Softcup (cervical) | Increase in enterococcus from cycle 2-cycle 3 (p=0·03 according to source) | “… this increased frequency persisted for 3 months after discontinuing use of the cup, suggesting that factors or behavior other than cup use may have influenced colonization.” Data in figure 3 in publication, can’t be extracted. | North and Oldham 201114 |
| *Escherichia coli* | Softcup (cervical) | According to authors, no significant changes from baseline-cycle 3 | Data in Figure 3 in publication, can’t be extracted | North and Oldham 201114 |
| *Escherichia coli* on menstrual cup | Mooncup (vaginal) | 13/35 randomly selected cups showed *E. coli* growth (37·1%). 9/17 (53%) if MC-use less than 6 months, 4/18 (22%) if MC-use > 6 months (p=0·12 from source). Association with heavy periods (61·5% vs. 22·7%, p=0·022 from source article, no numbers presented)  | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months. | Juma 201730 |
| *Chlamydia trachomatis* | Mooncup (vaginal) | Endline survey: cups 3/144 (2·1%), pads 3/201 (1·5%), usual item (control) 7/154 (4·5%). Cups vs. control: p=0·20, cup vs. pads p=0.63, p-values from source article. | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months.  | Phillips-Howard 20166 |
| *Trichomonas vaginalis* | Softcup (cervical) | Baseline, cycle 1-3: 0 cases | Sample sizes not reported. | North and Oldham 201114 |
| Mooncup (vaginal) | End line survey: cups 2/143 (1·4%), pads 5/200 (2·5%), usual item (control) 7/154 (4·5%). Cups vs. control: p=0·12, cup vs. pads p=0.36 (p-values from source article) | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months.  | Phillips-Howard 20166 |
| Ruby cup (vaginal) | 0/18 at enrolment, 0/18 at 3-5 months follow up |  | Tellier 201255 |
| *Neisseria gonorrhoea* | Mooncup (vaginal) | Endline survey: cups 1/144 (0·7%), pads 1/201 (0·5%), usual item (control) 1/154 (0·6%). Cups vs. control: p=0·96, cup vs. pads p=0.81, p-values from source article. | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months.  | Phillips-Howard 20166 |
| Ruby cup (vaginal) | 0/18 at enrolment, 0/18 at 3-5 months follow up |  | Tellier 201255 |
| *Staphylococcus aureus* | Softcup (cervical) | No significant changes in cycle 1-3 compared to baseline | Data in Figure 3 in publication, can’t be extracted  | North and Oldham 201114 |
| Mooncup (vaginal) | Among MC-users: 4/38 (10·5%) in 1st month of intervention, 13/139 9·4% after 1st month, p=0·83 (median follow up 4, range 2-11 months for this substudy).Prevalence in menstrual pads-arm 10·7% (21/197), usual item-arm 10·5% (16/153) | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months.Sample from vaginal swab (self-swabbing). | Juma 201730 |
| be’Cup (vaginal) | Silicone cup: potentially more *S. aureus* after incubation for 8 hours with shaking in plastic sac with *S. aureus* in one of two cups used, but not when no shaking | In-vitro studies | Nonfoux et al 201867 |
| Me Luna (vaginal) | Thermoplastic isomer cup: not more *S. aureus* after incubation for 8 hours with shaking in plastic sac, and not when no shaking | In-vitro studies | Nonfoux et al 201867 |
| Toxic shock syndrome toxin (TSST)-1 | Mooncup (vaginal) | 49 girls with vaginal *S. aureus* had second swab, 10 yielded *S. aureus*, 2 had TSST-1, both in sanitary pad group; they were asymptomatic | Cluster-randomized trial (schools). Median follow-up 11 months, range 3-15 months.Sample from vaginal swab (self-swabbing). | Juma 201730 |
| NR | No TSST-1 in supernatant of S. aureus cultivated for 24 hours (incubated aerobically in a still growth environment) in presence of elastic polymer MC (N=16 MCs)  | In-vitro studies | Tierno and Hanna 198974 |
| Tassaway (vaginal) | *S. aureus* MN8 produced no TSST-1 when grown in the presence of Tassaway (elastomeric polymer, n=6), washed or unwashed, no shaking, incubation overnight | In-vitro studies | Tierno and Hanna 199466 |
| be’Cup (vaginal) | Silicone cup: potentially more TSST-1 production after incubation for 8 hours with shaking in plastic sac with *S. aureus* compared to control, but not when no shaking or with pieces of cup | In-vitro studies | Nonfoux 201867 |
| Me Luna (vaginal) | Thermoplastic isomer cup: potentially more TSST-1 production after incubation for 8 hours with shaking in plastic sac with *S. aureus* compared to control, but not when no shaking or with pieces of cup | In-vitro studies | Nonfoux 201867 |
| Toxic shock syndrome | Mooncup (vaginal) | 0/192 in trial in Kenya | “Safety monitoring components comprised routine nurse-based screening, population-based monitoring (school and community) and clinical evaluation of infection with laboratory confir­mation.” Study in Kenya | Juma 201730 |
| Softcup (cervical) | 2 case reports FDA database | Both unconfirmed cases of TSS. | North and Oldham 201114 |
| Divacup (vaginal) | 1 case report; blood cultures and urine culture negative, no culture of the menstrual cup conducted. | Woman had history of Hashimoto’s thyroiditis and chronic menorrhagia. | Mitchell 201562 |
| Mooncup (vaginal) | Event February 2012: toxic shock syndrome two days after using of first and new mooncup resulting in 9 days of hospitalization. Vaginal swab positive for *S. aureus*.  | Had IUD. Mooncup not sent for bacteriological testing. Cases of TSS in association with IUD have been reported.81  | FDA Database15 |
| Divacup (vaginal) | Event February 2015: toxic shock syndrome from Streptococcus resulting in 5 days of hospitalization. Culture of cup isolated group A and B streptococcus.  | Woman had used divacup for menstrual period which started 3 days before illness. MC was in for 18 hours on admission. | FDA Database15 |
| Urinary tract infections (UTI) | Ruby cup (vaginal) | 4/31 (12·9%) at baseline and 3/18 (16·7%) at follow up (after 3-5 months) (p=0·65, McNemar test) | One participant with UTI at enrolment and follow up had her cup stolen and used toilet paper in vagina as tampon | Tellier 201255 |
| Gynaeseal (cervical) | 1/73 (1·4%) transient dysuria | “The woman who developed dysuria did not seek treatment and the problem subsided within 24-48 hours.” | Cattanach 199138 |
| Softcup (cervical) | Urine analysis conducted, detailed results not reported | “Monthly monitoring did not show adverse effects of MC-use” | North and Oldham 201114 |
| Softcup (cervical) | Reported August 2014: Urinary tract infection confirmed by urine cultures twice after use of softcup. | Medical records were not available for evaluation. | FDA Database15 |
| Infections overall | Tassette (vaginal) | “The amount of bacterial contamination was greatest with the pad, next with the tampon and least with the rubber cup.” | No data provided. Study reported to make cultures from vaginal wall samples and to examine fresh and stained smears for *C. albicans*, *T. vaginalis*, *H. vaginalis*, and for predominance of Gram-positive or Gram-negative cocci, small rods or long-rod bacilli (*Doederlein bacilli*). | Karnaky 196265 |
| Softcup (cervical) | FDA database 1 case report | Vaginal infection not further specified. Could not be confirmed at follow up. | North and Oldham 201114 |
| Butterfly cup (vaginal) | “None of the women sought treatment for a pelvic infection (follow up one year). There was no onset or worsening of dysmenorrhoea in 43 (83%), dyspareunia in 94% (49), pelvic pain in 92% (48) and vaginal discharge in 92% (48) of the participants during the 12 months of cup use.” n=52 |  | Madziyire 201848,69 |
| Gynaeseal | “There was no increased pathogenicity detected in the vaginal flora. There was a trend towards smaller numbers of potentially pathogenic bacteria for 4 women and no change for one woman.” | Vaginal swabs before and after use, n=5 adult women, median follow up 14 months | Cattanach 198939 |
| Sexually transmitted infections  | Mooncup (vaginal) | Endline survey: MCs 6/144 (4·2%), pads 9/202 (4·5%) and usual items (control) 12/156 (7·7%). MC vs. control: p=0·11, MC vs. pads p=0.87, p-values from source articleIf follow up ≥9 months: cups 4/101 (4·0%), pads 7/143 (4·9%) and usual item 11/104 (10·6%). MC vs. control: p=0·004, MC vs. pads p=0.60, p-values from source article. | Sexually transmitted infections: presence of either *C. trachomatis*, *T. vaginalis* or *N. gonorrhoea*. Cluster-randomized trial (schools) in Kenya. Median follow-up 11 months, range 3-15 months\* | Phillips-Howard 20166 |
| Reproductive tract infections | Mooncup (vaginal) | End line survey: cups 31/144 (21·5%), pads 58/202 (28·7%), and usual item (control) 42/156 (26·9%), MC vs. control: p=0·36, MC vs. pads p=0.19, p-values from source article | Reproductive tract infections: presence of either *B. vaginosis* or *C. albicans.*Cluster-randomized trial (schools) in Kenya. Median follow-up 11 months, range 3-15 months.  | Phillips-Howard 20166 |
| **Other Adverse events** |  |
| Urine incontinence | Femcap (first model of femmycycle, vaginal) | FDA database 1 case report. Event July 2014. Pelvic pain and urinary incontinence when wearing and removing MC. Urine sample negative for infection. | Self-report. Stopped using MC. | FDA Database15 |
| Displacement of intra-uterine device when using menstrual cup | NR | IUD expulsion within 6-8 weeks after insertion: MC-users: 5/135 (3·7%), tampon: 11/469 (2·4%), pads: 7/169 (4·1%). Cup vs. tampon: p=0·57, cup vs. pads: p=0·92 | Retrospective cohort. Expulsion of an IUD occurs in ~1 in 20 women and is most common in the first three months after insertion. Expulsion commonly occurs during menstruation.82 Some recommend not to use internal sanitary protection for 3-6 weeks after insertion because of an increased infection risk.83 | Wiebe and Trouton 201256 |
| Mooncup (vaginal) | FDA database 1 case report. Event July 2012. Potential IUD dislodgment after mooncup removal. Patient had an ectopic pregnancy and needed surgery. | Patient felt pain after removal of mooncup and had the position of the IUD checked at a health center where it was declared in position. Two months later she was found pregnant.  | FDA Database15 |
| NR | Case series of 7 women with IUD expulsion when removing MC. Expulsion occurred 1 week -13 months after insertion IUD and was recurrent in 2 women. Of 7 women, 2 choose for different anticonception; others had IUD re-inserted. | Two women opted for cutting the wires of IUD close to cervix to avoid the problem. Authors also stress importance of releasing vacuum of MC before removal.  | Seale 201973 |
| Endometriosis because of menstrual backflow through menstrual cup use | Tassette (vaginal) | Position cup confirmed using X-ray  | “The free space available in the upper vagina and the capacity of the cup itself are ample to accommodate several times the amount of blood passed in a complete menstrual cycle.” | Pena 196250 |
| Tassette (vaginal) | No evidence for backflow | "Thin watery solutions could not be introduced under high pressures during the menstrual flow in 6 multiparous women" | Karnaky 196265 |
| Keeper (vaginal) | Case report: dysmenorrhoea 2 years after start of menstrual cup use (10 years ago tubal ligation). Laparoscopy showed adenomyosis and endometriosis, treated with laser. Patient stopped MC-use; pain decreased postoperative; 2 years follow up.  | “The observation in our patient suggests that it may be useful to inquire about use of these devices in women with pelvic pain or endometriosis”. “…it may be prudent to advise women … to empty the menstrual cup more often than every 6-12 h….”Petition for revoking of market approval to Food and Drug Administration rejected because of lack of evidence.84 | Spechler 200364 |
| Hydronephrosis,renal colic | NR | Case report: Severe colicky flank pain. CT-scan: Menstrual cup slightly dislocated, pressing to left ureter | “The extraction of the menstrual cup resulted in resolution of hydronephrosis and associated symptoms” | Adedokun 201758 |
| NR | Case report: Three hours back pain right side. Low-dose unenhanced CT-scan: entrapment of left vaginal wall and part of interolateral bladder wall. Improperly positioned MC | Symptoms and swelling vanished after removal of MC, confirmed by new scan. Patient was long time MC-user. No previous MC problems, and continued use of MC, no problems at follow up after several weeks.  | Stolz 201972 |
| NR | Case report: Three hours pain right flank, nausea menstruation. X-ray: MC orientated to the right | “The symptoms and the ureterohydronephrosis relieved completely after the removal of the device.” Patient had used MC for two years | Nunes-Carneiro 201859 |

Note: Entries in FDA database61 for softcup not entered if before 2011, to avoid double reporting with North and Oldham (2011).13

\*The reduction of sexually transmitted infections in this trial in Kenya in the arms where either MCs or sanitary pads were provided is thought to be an indirect effect because of the reduction of risky sexual behaviour to obtain resources to deal with menstruation.

***Table 3:* Summary table of pooled estimates of meta-analyses for different outcomes of acceptability**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Pooled prevalence (%),** **95% CI** | **Number of studies (or subgroups)** | **Total participants** | ***I2*** | **p-value for heterogeneity** | **p-value for z-test†** |
| Could not insert cup | 2.8, 0.8-5.6 | 11 | 1251 | 79.3% | <0.0001 | 0.0002 |
| Use MC at least once (verbal report) | 79.3, 68.5-88.4 | 25 | 2367 | 97.1% | <0.0001 | <0.0001 |
| MC-related discontinuation | 10.7, 2.7-22.6 | 10 | 1190 | 96.4% | <0.0001 | 0.0004 |
| Other discontinuations | 9.0, 3.8-15.9 | 15 | 1783 | 94.9% | <0.0001 | <0.0001 |
| Difficult to insert (among users) | 20.3, 11.7-30.4 | 17 | 1061 | 92.3% | <0.0001 | <0.0001 |
|  First cycle | 35.3, 15.4-58.1 | 5 | 272  | 92.7% | <0.0001 | <0.0001 |
|  Later cycles\* | 13.0, 8.1-18.7 | 12 | 789 | 74.3% | <0.0001 | <0.0001 |
| Uncomfortable to wear | 12.6, 5.9-21.3 | 12 | 958 | 91.9% | <0.0001 | <0.0001 |
|  First cycle | 32.9, 2.2-76.2 | 3 | 221 | 97.5% | <0.0001 | 0.0148 |
|  Later cycles\* | 7.9, 4.0-12.9 | 9 | 737 | 77.1% | <0.0001 | <0.0001 |
| Difficulty removing | 9.3, 2.9-18.3 | 7 | 461 | 84.7% | <0.0001 | 0.0001 |
| Continue using the cup | 72.5, 59.0-84.3 | 15 | 1144 | 95.6% | <0.0001 | <0.0001 |
|  Study before 2000 | 68.5, 16.1-100.0 | 4 | 241 | 98.4% | <0.0001 | 0.0014 |
|  Study after 2000\* | 73.8, 63.0-83.3 | 11 | 903 | 91.5% | <0.0001 | 0.0001 |

Note: There was no significant difference for any of the subgroup analyses (high vs. low-middle income countries, adult women vs. adolescents, type of cup, duration of follow up, or high vs. low/moderate study quality). For small-study effect see appendix page 23.

\*Difficult to insert: First vs. later cycles: p=0.15. Uncomfortable to wear: First vs. later cycles: p=0.13, Continue to use cup: before vs. after 2000: p=0.29

†z-test: A significant z-test indicates that the pooled prevalence is different from zero

**Figure 1. Flow diagram**



\*Reference lists of relevant studies, websites of pertinent professional bodies (e.g. FDA), non-governmental organizations and ‘grey literature’ (e.g.,reports or conference abstracts) and records recommended by experts. Last search date 14 May 2019

***Figure 2:* Menstrual cup and leakage**

***2A:* Proportion of leakage in seven studies using different types of menstrual cups and definitions**



***2B:* Complaint of leakage among menstrual cup users versus users of other menstrual products**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Study type** | **Comparison** | **Outcome** | **Menstrual Cup** | **Alternative** | **p-value** |
| Cheng 199542 | Observational, before-after | Valve Cup vs. usual item\* | Leakage after 1 MC cycle vs. leakage with usual product | 23/51 (45·1%) | 33/51 (64·7%) | † |
| Beksinska 201520 | Trial, cross-over | Vaginal cup vs. usual item\* | Complaint of leakage (3 cycles) | 3/106 (2·8%) | 1/104 (1·0%) | † |
| Howard 201124 | Trial, individually randomized | Vaginal cup vs. tampon | Mean Likert score for leaking‡ (3 cycles) | 5·4, sd 1·4 n=45 | 4·8, sd 1·5, n=44 | 0·04 § |
| Stewart 201052 | Observational, before-after | Vaginal cup vs. usual item\* | Mean number of leakage episodes per cycle (3 cycles per item) | 1·2 (83/71 cycles) | 1·7 (209/126 cycles) | † |

Abbreviations: sd=standard deviation. MC=menstrual cup.

\* Disposable pad or tampon.

† No p-value provided in source material.

‡ Likert scale: 7-point score, whereby 1 = terrible and 7 = great.

§ P-value reported in article for Mann-Whitney test.

***Figure 3:*** **Proportion of women who wanted to continue menstrual cup use after the study, in studies before and after the year 2000**



Notes: All studies in this graph used vaginal cups. In the study of Cheng et al (1995),42 a cup with a valve in the stem was used. In the study by Parker et al (1966),49 one study population had menorrhagia (n=46) and the other population had normal flow (n=19).