

Community-based distribution of misoprostol for the prevention of postpartum hemorrhage: misconceptions related to misuse and diversion of facility birth

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Abstract

Introduction : In low-resource settings, most maternal deaths caused by hemorrhage, occur in poorly resourced facilities or outside of health facilities where there is no access to skilled obstetric care. Community distribution of misoprostol is one of the compelling strategies for preventing or treating postpartum hemorrhage to avert maternal deaths. This scoping review was conducted to synthesize existing evidence that shows the negative impact of community distribution of misoprostol on facility delivery and misuse for labor induction or pregnancy termination. **Methods:** We identified and included all peer-reviewed articles on misoprostol implementation from PubMed, Cochrane Review Library, Popline, and Google Scholars. Narrative synthesis was used to analyze and interpret the findings in which quantitative and qualitative syntheses are integrated. **Results:** Three qualitative studies, six observational studies, and four experimental or quasi-experimental studies from Africa and Asia are included in this study. All before-after household surveys reported, increased delivery coverage after the intervention: ranging from 4 to 46 percentage points at the end of the intervention when compared to the baseline (5 studies). The pooled analysis of experimental and quasi-experimental involving 7,564 women from four of the studies revealed that there is no significant difference in facility delivery among the misoprostol and control groups [OR 1.011; 95% CI: 0.906-1.129]. A qualitative study among professionals also indicated that community distribution of misoprostol for the prevention of postpartum hemorrhage is acceptable to community members and stakeholders and it is a feasible interim solution until access to facility birth is improved. In the community-based distribution of misoprostol programs, administration of misoprostol before delivery was reported in less than 2% among seven studies involving 11,108 mothers. Evidence also shows that most women used misoprostol pills as instructed. No adverse outcomes from misuse in either of the studies reviewed. **Conclusions:** The claim that community-based distribution of misoprostol would divert institutional delivery strategies to home deliveries and promote misuse are not supported with evidence. Therefore, community-based distribution of misoprostol can be an appropriate strategy for reducing maternal deaths which occur due to postpartum hemorrhages especially in resource-limited settings where many deliveries take place outside of health facilities.

Introduction

Maternal mortality ratio (MMR) remains high in low-and-middle-income countries (LMICs) and continues to be a priority challenge in the Sustainable Development Goals (SDG) era [1]. Accordingly, to achieve the SDG of reducing the global MMR to 70 per 100,000 live births by 2030, LMICs needs to implement innovative and high impact interventions that aim at preventing and managing the main causes of maternal deaths and providing high-quality services in the continuum of maternity care [2, 3].

A wealth of evidence shows that hemorrhage is one of the major causes of maternal mortality [4-7]. More than two-thirds of maternal deaths due to hemorrhage occur during the postpartum period that accounts for a quarter of all maternal deaths [8, 9, 6]. Reports also show that postpartum hemorrhage (PPH) accounts for 15 % of maternal deaths in sub-Saharan African [6]. In Ethiopia, a systematic review of national evidence shows that PPH accounts for 30% of maternal deaths [10, 11].

Most maternal deaths occurring due to PPH are in poorly resourced facilities or outside of a health facility where there is no access to skilled obstetric care [8, 12, 13]. Women who deliver at home face the highest risk of PPH as they do not benefit from the support of skilled birth attendants and are less likely to receive timely care and medications that prevent PPH [13]. Evidence shows that most PPH-associated deaths could be avoided if active management of third stage of labor (AMTSL) is implemented [14], adverse outcomes and complications are prevented or managed using safe drugs at community and facilities, and effective referral mechanism institutionalized during delivery and postpartum period [9].

Misoprostol distribution at community level is one of the effective interventions for preventing or treating PPH. Misoprostol has been studied in different setups and is endorsed by the World Health Organization (WHO) as a solution for women who give birth in facilities without oxytocin or where there is low coverage of skilled attendance [15]. Clinical trials reveal the effectiveness and safety of community distribution of misoprostol [9, 16-18] where access to skilled birth attendance and oxytocin is limited.

However, community-based distribution of misoprostol is still the least prioritized intervention in the maternal survival strategies [19-23] due to concerns of policymakers' and practitioners' [18, 17, 23, 13] that misoprostol distribution at community level might decrease facility deliveries, possibility of misuse of misoprostol (taking the drug before delivery and using the drug for the purpose of inducing abortion), and lack of technologies and expertise to diagnose multiple pregnancies before using it at community levels in resource-limited settings [16, 24]. Thus, a range of barriers are engrained in the health system and community and policy level impede access to misoprostol for prevention and/or

treatment of PPH due to: 1) absence of registration of misoprostol for the management of PPH [25, 23], 2) fear and apprehensions of providers and policymakers regarding its use [25, 23], 3) lack of evidence-based guidelines and provider training [23], and 4) inadequate staffing and lack of knowledge and skill of providers regarding causes of PPH and limited knowledge of the community regarding the dosage and timing of administration [25, 16].

This scoping review was, therefore, conducted to synthesize existing evidence of whether community distribution of misoprostol negatively impacts utilization of facility delivery and results in misuse and increases risk of adverse pregnancy outcomes.

Methods

Criteria for inclusion

In this study, researchers used a scoping review methodology to get a wide range of information from both qualitative and quantitative studies. All types of literature on community-distribution of misoprostol for the prevention and/or treatment of PPH reported in English language with no specification on duration of publication were consulted.

Search strategy

We identified peer-reviewed articles on misoprostol implementation from PubMed, Cochrane Review Library, Popline, and Google Scholars which were made available until February 15, 2019. We also applied a snowball approach of searching from the references of papers of the initial search.

The following search strategy was used to search literature from PubMed and CENTRAL databases;

“((((((((((((Africa OR Asia OR Caribbean OR West Indies OR South America OR Latin America OR Central America OR Middle East))) OR ((developing countr OR less developed country * OR under developed country * OR underdeveloped country * OR middle income country * OR low income countr*)))))) AND (((postpartum hemorrhage) OR post partum hemorrhage) OR postpartum haemorrhage) OR post partum*

haemorrhage)) AND misoprostol)) AND (((community distribution) OR community) OR community based))) AND (((adverse effects) OR adverse outcomes)) OR ((misuse) OR ("Drug Misuse"[Mesh] OR "Prescription Drug Misuse"[Mesh])) OR (((skilled delivery) OR institutional delivery) OR "Delivery, Obstetric"[Mesh] OR delivery))”

Moreover, a combination of terms, including ‘misoprostol’; ‘misuse ’; ‘adverse outcomes’; ‘fear of diversion of facility birth’; ‘misconceptions’; ‘misperceptions’; ‘post-partum hemorrhage’ (and variations i.e. ‘post-partum hemorrhage’, ‘postpartum hemorrhage’); ‘community-based maternal’; ‘maternal health interventions’; ‘maternal mortality’; and ‘low-income setting’, ‘developing country’, ‘resource-poor setting’ have been used to identify the required literature from Popline and Google Scholar.

First, any research output with the above-mentioned terms in either the title or abstract of the article is downloaded, and then a combination of these terms was also used to download more resources.

Data extraction and analysis

The form for abstracting data from reviewed literature was designed and review team members agreed on the contents of the form. Two reviewers (GT and YT) read each identified literature and populated the sheet designed for the purpose. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (Figure 1) was used for the selection of articles to be used in this scoping review.

Figure 1: Study flow diagram

Facility delivery rate, misuse, adverse effects from misuse of the drug, and misconceptions on the use of misoprostol and fear of diversion of facility delivery to home delivery because of misoprostol’s access to mothers were the main points considered in this scoping systematic review.

In this study, a narrative synthesis was used to analyze and interpret the findings in which quantitative and qualitative syntheses are integrated. Descriptive information about the eligible studies was summarized using text and tables. Findings from the quantitative resources were narrated thematically followed by findings of qualitative resources. For

intervention studies, a random-effects meta-analysis model [26, 27] was used to pool the estimates of the facility birth outcome, accounting for the variability among studies using Stata v15 [28]. The results were presented as average treatment effects (odds ratio) with 95% confidence intervals.

Results

Description of studies

Table 1 presents the characteristics of the studies included in this review. Seven of the studies were from Africa and the remaining seven were from Asia. Three qualitative studies [29, 24, 13], six observational studies [30-35], and four experimental or quasi-experimental studies [36-39] were included in this study.

Table 1: Characteristics of included studies

Study ID	Country	Study design	Objectives	Description of the intervention	Outcome
Geller 2014	Ghana	Before-after intervention and comparison facility-based study	Assess the safety, feasibility, and acceptability of community-based distribution of misoprostol to prevent PPH during home deliveries in rural areas	Misoprostol distributed to midwives at seven primary health centers for provision to pregnant women	<ul style="list-style-type: none"> • No evidence of misuse; • Misoprostol distribution did not encourage home deliveries; • Regional household surveys showed that deliveries with skilled providers increased from 30 to 69%.
Haver 2016	Afghanistan	before-and-after cross-sectional household surveys	To determine the effectiveness of advance distribution of misoprostol for self-administration across 20 districts and identify any adverse events that occurred during expansion	Community health workers (CHWs) did advance distribution of misoprostol Interventions: 1) CHWs visited households; 2) community health councils were engaged to raise awareness of misoprostol for prevention of postpartum hemorrhage, and 3) health facility intrapartum services	<ul style="list-style-type: none"> • 1 out of 7,399 women in the study reported taking misoprostol before the birth of her newborn • No maternal deaths attributable to misoprostol • Increased proportion of women who gave birth in a facility after the intervention (from 50.2% to 60.8%); the intervention did not discourage women from receiving skilled birth attendance

Study ID	Country	Study design	Objectives	Description of the intervention	Outcome
Rajbhandari 2010	Nepal	Before-after household survey	To determine feasibility of community-based distribution of misoprostol (for preventing PPH) to pregnant woman, through community volunteers	Support and training to peripheral health workers and female community volunteers to enable them to: identify pregnant women in their area, provide prenatal health education, dispense misoprostol late in pregnancy, and make early postnatal home visits	The institutional delivery rate among live births increased from 10.9% at baseline to 14.8% at end line
Sanghvi 2010	Afghanistan	Non-randomized experimental control design	To test the safety, acceptability, feasibility, and effectiveness of community-based education and distribution of misoprostol for prevention of postpartum hemorrhage during home birth	In both the intervention and comparison areas, CHWs made 3 home visits to pregnant women and their families: CHWs used pictorial flipcharts to provide education on birth preparedness and complication readiness; and recognition of danger signs	Significant number of women delivered in facilities ($p < 0.001$): 21% and 18% of births took place at health facilities in the intervention and comparison areas respectively.
Weeks 2015	Uganda	Community-based placebo-randomized controlled trial (RCT)	Examine safety and effectiveness of self-administration of misoprostol by women	Women were randomized into misoprostol or placebo group during their third trimester ANC visit and they were instructed to take immediately after childbirth before the delivery of the placenta, and after confirming the absence of a twin, if they delivered at home.	Facility delivery: 56.5% in the misoprostol group vs 58.2% in the placebo group

Study ID	Country	Study design	Objectives	Description of the intervention	Outcome
Smith 2014	Liberia	Longitudinal observational study	Evaluate the feasibility, acceptability, effectiveness of advance distribution of misoprostol during ANC and home visits	Trained traditional midwives as CHWs provided education to pregnant women, and district reproductive health supervisors distributed misoprostol during home visits	Misoprostol taken before delivery of baby; 3 (1.1%) Based on Health Management Information System data, ANC1 and ANC4 appears to be unchanged, while, the average monthly number of facility deliveries increased from the 82 during the comparison period (same period in the previous year) to 108 during the intervention period
Ononge 2015	Uganda	Cluster RCT	To determine if antenatal distribution of misoprostol to pregnant women to self-administer at home birth, reduces PPH	Women at 28+ weeks of gestation attending antenatal care were offered misoprostol to swallow immediately after birth of baby when oxytocin was not available	<ul style="list-style-type: none"> No woman took misoprostol before their baby's birth. No difference in postpartum anemia, uterotonic use, and facility births (85.4% I vs 87.5 % C group)
Durham 2018	Lao People's Democratic Republic	Qualitative study IDI, n=25 & FGDs, n=5	Identify acceptability of misoprostol and healthcare system needs to effectively distribute misoprostol to women with limited access to facility-based birthing	NA	All healthcare professionals interviewed recognized that community distribution of misoprostol is an acceptable and feasible interim preventative solution to reduce PPH until access to facility-based birthing is improved

Study ID	Country	Study design	Objectives	Description of the intervention	Outcome
Spangler et al 2014	Ethiopia	Qualitative in-depth interviews	The purpose of this study was to examine the understanding of national policy for community-based use of misoprostol to prevent PPH	NA	Among all officials, understandings of national policy for community-based PPH prevention using misoprostol were unclear.
Wells et al 2016	Ethiopia, Ghana,	Desk review and qualitative methods	Evaluated the models and approaches used to access misoprostol at the community level in Ethiopia, Ghana, and Nigeria	NA	<ul style="list-style-type: none"> • There is pervasive lack of trust in women's capabilities to use misoprostol correctly and the widely held belief that women might "misuse" the pills (for abortion) persist • Fears that providers will inappropriately use misoprostol for labor induction and/or abortion
Sibley 2014	Ethiopia	Before-and-after household design; facility records	Describes regional trends in women's use of misoprostol; their awareness, receipt, and use of misoprostol at project's end line; and factors associated with its use	Community health development agents and TBAs conducted community maternal and newborn health family meetings with pregnant women and their family caregivers. Distributed misoprostol tablets to the project area woreda health offices, to distribute either through HEWs (in Amhara) or TBAs (Oromia)	<ul style="list-style-type: none"> • Controlling for age, parity, and education, region, any ANC, and any CMNH family meeting attendance, a woman's receipt of misoprostol during pregnancy was not significantly associated with place of birth (OR= 0.64; 95% CI, 0.35-1.19). • Very few women consumed the tablets before birth (~2%)

Study ID	Country	Study design	Objectives	Description of the intervention	Outcome
Rajbhandari 2017	Nepal	Mixed methods program evaluation	This paper presents findings from the first large-scale assessment of the effectiveness of the advance distribution program.		<ul style="list-style-type: none"> • High rate of institutional delivery; • No evidence that misoprostol was used for any other purpose (including labor induction and abortion). • The majority of those who did not use their advance misoprostol returned it after the birth and most others either threw it away or kept it.
Parashar 2018	India	Cross-sectional program evaluation	To design and implement an operational framework to implement and scale up “Community Based Advance Distribution of Misoprostol” program in India	Community-based distribution of misoprostol to pregnant women on completion of the 8th month of their pregnancy, in identified high home delivery geographical pockets and women who are likely to deliver at home	The institutional delivery rate in the area increased from 11 to 57% within six months of implementation
Derman 2006	India	RCT	To investigate whether oral misoprostol, a potential alternative to oxytocin, could prevent PPH in a community home-birth setting	25 auxiliary nurse midwives undertook the deliveries, administered the study drug, and measured blood loss	Institutional delivery rate: 53.2% in the intervention group vs 54.8% in comparison group

The results of our review are presented under three sections: 1) diversion of facility birth, 2) misuse, for purposes of either abortion or labor induction/augmentation, and 3) adverse events from misuse.

Diversion of facility birth

Ten studies (five observational before-after studies, four experimental or quasi-experimental trials, and one qualitative study) reported on the facility birth outcome [32, 33, 36, 31, 37, 30, 35, 29, 38, 39]. All five before-after household surveys reported increased delivery coverage after the intervention: four percentage points increase in Nepal [33] and Liberia [32], 11% points in Afghanistan [31], 39% points in Ghana [30], and 46% points in India [35] at the end of the intervention when compared to the baseline (Figure 2).

Figure 2: Changes in facility delivery rate before and after the intervention

A quasi-experimental study in Afghanistan demonstrated an increase of 3.3 percentage points in facility birth rates comparing between the intervention and control areas; however, a randomized controlled trial (RCT) in India showed a decrease by 1.6 percentage points and two cluster randomized trials in Uganda showed a decrease of 1.5 and 2.1 percentage points in facility birth rates, comparing between the intervention and control areas [36, 38, 39]. The pooled analysis involving 7,564 women, from four of the studies, revealed that there is no significant difference in facility delivery among the misoprostol and control groups [OR 1.011; 95% CI: 0.906-1.129] (Table 2).

Table 2: Comparison of facility delivery rates between the intervention and control areas

Study	Facility delivery rate (%)		OR	[95% CI]		% Weight
	Intervention	Comparison				
Sanghvi 2010	21.4	18.1	1.229	1.023	1.477	35.93
Weeks 2015	56.5	58.0	0.940	0.697	1.269	13.52
Ononge 2015	85.4	87.5	0.834	0.647	1.075	18.80
Derman 2006	53.2	54.8	0.937	0.770	1.139	31.76
I-V pooled OR			1.011	0.906	1.129	100.0

A qualitative study among professionals also indicated that community distribution of misoprostol, for the prevention of PPH, is acceptable to community members and stakeholders and it is a feasible interim solution until access to facility birth is improved. The study recognized misconceptions as barriers that might hinder community-based distribution of misoprostol [29]. Another study in Ethiopia reported regional differences in understanding the implementation strategy of misoprostol and a different concern among policymakers – that is fear of encouraging home birth [24].

Misuse

A program evaluation report in Nepal showed that there was no evidence to suggest that misoprostol distributed for the purpose of the prevention of PPH is being diverted for labor induction or pregnancy termination [40]. Moreover, as presented in Table 3, in the community-based distribution of misoprostol programs, administration of misoprostol before delivery was reported in less than 2% (n=17) among seven studies involving 11,108 mothers [30, 31, 34, 32, 38].

A cluster randomized controlled trial in Uganda [38] and an operations research in Ghana [30] reported that no woman took misoprostol before their babies' birth. Another before-after study in Afghanistan reported that only one out of 7,399 women in the study take misoprostol before the birth of her newborn [31]. Similarly, according to a trial in Uganda, only two out of 700 women took tablets before delivery [36]. In Liberia, only three of 265 women took misoprostol prior to giving birth [32]; while in Ethiopia, less than 2% of women took the tablets before birth [34] (Table 3).

Table 3: Percent of women who took misoprostol before delivery

<i>Study ID</i>	<i>Country</i>	<i>%</i>	<i>n</i>	<i>N</i>
Geller 2014	Ghana	0.00	0	102
Ononge 2015	Uganda	0.00	0	2,057
Haver 2016	Afghanistan	0.01	1	7,399
Weeks 2015	Uganda	0.29	2	700
Smith 2014	Liberia	1.10	3	265
Sibley 2014	Ethiopia	1.80	11	585
Total			17	11,108

Evidence also shows that most women used the misoprostol pills as instructed [33, 30, 39]; unused doses were returned after birth to the point of distribution; and most others either threw it away or kept it [30, 40]. However, qualitative studies in Ethiopia identified, lack of trust in women’s capabilities to use misoprostol correctly [13] and fear of misuse [13, 24], as a problem.

Adverse effects of misuse

No adverse outcomes of misuse were reported in either of the studies reviewed.

Discussion

This review shows that misoprostol community-based distribution programs demonstrated increments in coverage of facility-based births. The studies reviewed also find very few rates of administration of misoprostol before delivery and no adverse outcomes because of misuse. Despite the apparent prevailing fear of misoprostol misuse, diversion of facility birth, and adverse effects of its misuse [13, 24, 19]; this scoping review showed that, so far, community-based distribution of misoprostol did not negatively impact facility birth and did not promote misuse. Accordingly, the apparent prevailing fear of misoprostol misuse, diversion of facility birth, and adverse effects of its misuse are simply misconceptions and there is no evidence that supports the claim. As it is evident from a qualitative study in Ethiopia [24], these misconceptions arise from the health providers’ perception but not from the women using misoprostol.

In addition, evidence shows that misoprostol is safe and effective for preventing and treating PPH in remote settings where both oxytocin and timely transfer to higher-level care are not available [41, 18, 23]. Previous studies also report that community health workers or other lower-level workers could safely administer misoprostol [15, 29]. Women were found to have no major problem of misusing the drug and it was found to be acceptable by them [15]. Another rapid review of the literature showed that distribution of misoprostol in advance by lay health workers or self-administration were feasible and acceptable at all levels—end-user, health system, community, and policy [16, 23].

However, there are concerns by policymakers, often unsupported by available evidence [23], about misoprostol distribution at community level that impede the strategy to be translated into effective policies, programs, and practice. The concerns are, fear of women using misoprostol for inducing abortion or labor and diversion of facility-based birth strategies to home deliveries [36, 42, 23]. A range of barriers including service delivery challenges, supply and procurement, financial, national and global policy environments, and those factors more closely connected to the end-user that impede access to a uterotonic for prevention and/or treatment of PPH for every woman [43]. These implementation barriers represent important threats to any community-based program and most of these barriers reflect existing health system weaknesses in many countries [16].

Community-based distribution of misoprostol is a compelling strategy parallel to strengthening healthcare facilities to increase institutional deliveries [19, 23] to ensure universal access to uterotonics for every woman. A review by Hobday et al. recommends to simultaneously promote facility delivery and strengthen health systems to avail misoprostol at the community level [15]. It means, it is a complementary strategy for simultaneously increasing the availability of misoprostol and actively promoting facility births through increasing contact with pregnant women. And, their interaction offers the opportunity to promote early care-seeking and referral during pregnancy [16]. As such, the community-based distribution of misoprostol, then, should include the promotion of facility-based birth [5, 30, 29] as a critical intervention. Successful implementation of the misoprostol distribution can be ensured by providing enabling environment through supportive policies, designing a formal plan for supplies, task shifting strategies and appropriate use of guidelines and protocols [25]. Moreover, strong leadership and political commitment, training, and community mobilization were identified as critical success factors [16].

This study provides critical information gaps to help policymakers and program managers to develop national policies and to strategize the implementation of community-based distribution of misoprostol to prevent PPH and reduce maternal mortality. It also suggests that the rates of administration of misoprostol before delivery and adverse outcomes of misuse of community-based distribution of misoprostol for home births are very low,

especially when compared to the risks women encountered without access to uterotonic. As such, community-based distribution of misoprostol is an appropriate strategy till facility delivery becomes a norm.

However, decision-makers are still reluctant and have encountered dilemmas of ethical decision to implement this strategy. National guidance and policies from higher level of the health system as well as creating opportunities for reflective discussions or policy dialogue, is thus important for virtuous public health practice.

Implementation research is needed to examine implementation challenges as well as to continually demystify the concerns regarding misuse of the drug. Close monitoring is also critical as part of the implementation of the strategy. Further research is needed on how community-based distribution of misoprostol would be effective in hard-to-reach areas where most women give birth at home and are areas characterized by weak health system, poor community health workers' performance, mobile lifestyle, and poor infrastructure.

Conclusions

Community-based distribution of misoprostol programs demonstrated an increase in coverage of facility-based births. This review also finds very few rates of administration of misoprostol before delivery and no adverse outcomes of misuse in either of the studies reviewed.

Fears of misuse of misoprostol and increased adverse pregnancy outcomes if distributed at community, are not supported by evidence. Therefore, community-based distribution of misoprostol can be an appropriate strategy for reducing maternal deaths caused by postpartum hemorrhages, especially in resource-limited settings where many deliveries take place outside of health facilities.

Abbreviations

[Abbreviations](#)

AMTSL	Active Management of Third Stage of Labor
CHW	Community Health Workers
MoH	Ministry of Health
PPH	Postpartum Hemorrhage
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RAC	Research Advisory Council
RCT	Randomized Controlled Trial
RMNCAH-N	Reproductive, Maternal, Newborn, Child, Adolescent Health, and Nutrition
WHO	World Health Organization

Declarations

Ethics Approval and Consent to Participate

Not applicable

Consent for Publication

Not applicable

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

GT, BT, WM, YT, and AM conceptualized the paper. GT, MY, EG, and YT performed article search, data extraction, and data analysis. GT, BY, AM, WM, YT did interpretation and critical review. All authors contributed to the interpretation, commented on multiple versions, and approved the final manuscript.

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Figures

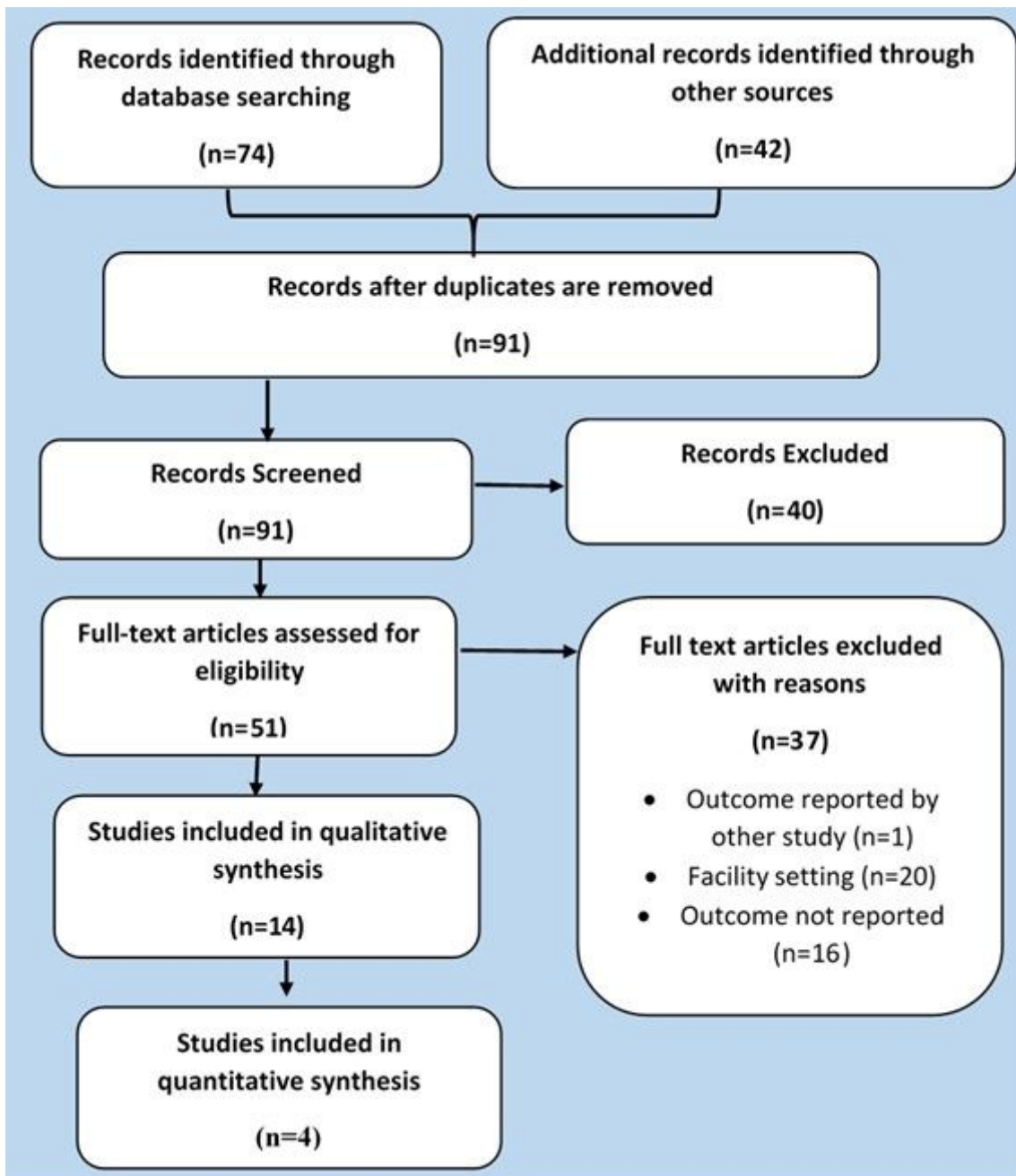


Figure 1

Study flow diagram

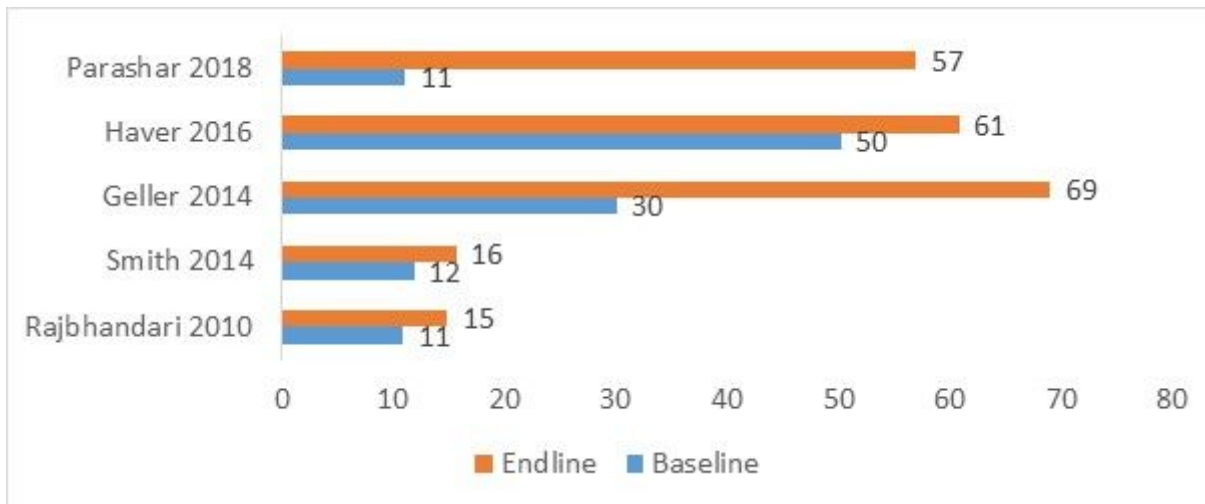


Figure 2

Changes in facility delivery rate before and after the intervention