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Commentary

Medical abortion reporting of efficacy: the MARE guidelines☆,☆☆

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1. Introduction

This commentary introduces the Medical Abortion Reporting of Efficacy (MARE) guidelines as a supplement to CONSORT [1] and STROBE [2]. The goal of the recommendations is to standardize early medical abortion efficacy reporting to facilitate comparison of outcomes between studies and to enrich the ability for data synthesis from different studies to create evidence-based guidelines. Although the term *medical abortion* had most commonly referred to the use of abortion-inducing medication for early pregnancy termination without primary surgical intervention, more recently, the phrase has been used to refer to labor induction abortions as well [3,4]. Accordingly, we consider early medical abortion to refer to procedures in the first trimester.

Reports of using medical agents to cause early abortion first appeared in the 1950s [5], but the modern era of medical abortion research started in the early 1980s with the discovery of test agents that were ultimately developed into mifepristone. Over the past 30 years, research has evolved, with the use of various drugs including mifepristone, methotrexate, tamoxifen, letrozole and various prostaglandin analogs to induce early abortion [6]. The first drug with a labeled indication for medical abortion, mifepristone, was initially approved in China and France more than two decades ago. The United States Food and Drug Administration approved mifepristone in 2000 for use in combination with the prostaglandin analog misoprostol for abortion through 49 days gestation.

Over the more than 25 years since mifepristone first became available for women to obtain a medical abortion, researchers have continued to evaluate alternative regimens to improve efficacy and the patient experience. Professional and national organizations now lead the way in promoting the best science by providing evidence-based recommendations for the preferred medical abortion treatment options [6–8]. Although many individual studies are methodologically strong, the heterogeneity of design, conduct and reporting hinders synthesis of data from multiple studies. Importantly, many studies do not stratify outcomes by week of gestation. These issues became evident during data collation for creation of the 2014 Medical Management of First Trimester Abortion Practice Bulletin written collaboratively by the American College of Obstetricians and Gynecologists and the Society of Family Planning [6,7]. More recently, a systematic review including approximately 30,000 patients who received mifepristone and buccal misoprostol found that only 57% had data identifying week of gestation for a stratified evaluation of overall efficacy; only 51% had such information for evaluation of continuing pregnancy [9].

Well-performed and reported research trials provide the basis for evidence-based guidelines and do more than simply inform providers and patients about more cost-effective or therapeutically effective options — they also affect access to care. Methodologically strong research can counter ideologically motivated arguments for legal restrictions on medical abortion regimens and gestational age limits. The medical community can use this evidence to oppose such legislation.

Future synthesis of the large body of available data to inform patient care and regulatory policy can be facilitated with the use of guidelines to ensure that publications of original data are presented in a standardized way. We herein present reporting recommendations for early medical abortion as a supplement to the CONSORT guidelines (for

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Table 1
The CONSORT supplement checklist for early MARE (MARE-C)

Section/Topic	Item No	Checklist item	Supplement for MARE	Reported on page #
TITLE AND ABSTRACT				
	1a	Identification as a randomized trial in the title		
	1b	Structured summary of trial design, methods, results, and conclusions		
INTRODUCTION				
Background and objectives	2a	Scientific background and explanation of rationale		
	2b	Specific objectives or hypotheses		
METHODS				
Trial design	3a	Description of trial design including allocation ratio		
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		
Participants	4a	Eligibility criteria for participants	4a-1 Detail the range of gestational age for participants determined a priori to be included in the research, including a lower limit when applicable.	
			4a-2 Explain the methods used to determine gestational age (e.g., physical examination, last menstrual period, ultrasonography). If ultrasonography is used, detail the type (vaginal and/or abdominal) and consider describing the criteria used for determination of gestational age.	
	4b	Settings and locations where the data were collected		
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Detail the medications used, including dose(s) and route(s) of administration. If more than one medication is used, state the planned time interval between medications, preferably in hours.	
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6a-1 Outcome: Define successful medical abortion (should most commonly be considered as successful expulsion of the intrauterine pregnancy without need for surgical intervention).	
			6a-2 Outcome: Define the types of medical abortion failure (e.g., ongoing pregnancy, incomplete abortion, participant symptoms). Continuing pregnancy should be defined as a viable pregnancy following treatment (to be differentiated from a non-viable [i.e., retained gestational sac]).	
			6a-3 Assessment: Explain the follow-up assessments used to determine outcome (e.g., urine pregnancy test, serum pregnancy test, ultrasonography, physical exam, symptoms checklists).	
			6a-4 Assessment: Explain the length of time planned to follow participants for determination of outcomes.	
	6b	Any changes to trial outcomes after the trial commenced, with reasons		
Sample size	7a	How sample size was determined		
	7b	When applicable, explanation of any interim analyses and stopping guidelines		
RANDOMIZATION				
Sequence generation	8a	Method used to generate the random allocation sequence		
	8b	Type of randomization; details of any restriction (such as blocking and block size)		
Allocation concealment	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned		
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions		

Table 1 (*continued*)

Section/Topic	Item No	Checklist item	Supplement for MARE	Reported on page #
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		
	11b	If relevant, description of the similarity of interventions		
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes		
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		
RESULTS				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	13a-1 Report the number of participants who started medical abortion treatment and the number who did not complete any follow-up for each group overall and by gestational age.*	
			13a-2 Report the number of participants used in the denominator for outcome evaluations for each group overall and by gestational age*, which most commonly will be the number of women with any follow-up.	
			13a-3 Include a description of the number of women who used the drug(s) as planned in the protocol (treatment adherence).	
			13a-4 When more than one drug is used (e.g. mifepristone and a prostaglandin analog), the actual time interval between the agents should be reported, preferably in hours.	
	13b	For each group, losses and exclusions after randomization, together with reasons		
Recruitment	14a	Dates defining the periods of recruitment and follow-up		
	14b	Why the trial ended or was stopped		
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group		
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups		
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	17a-1 Present treatment success for each group overall and by gestational age.*	
			17a-2 Present continuing pregnancies for each group overall and by gestational age.*	
			17a-3 Present reasons for surgical intervention other than continuing pregnancy for each group overall and by gestational age.*	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		
Harms	19	All important harms or unintended effects in each group		
DISCUSSION				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		
Generalizability	21	Generalizability (external validity, applicability) of the trial findings		
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relative evidence		

(continued on next page)

Table 1 (*continued*)

Section/Topic	Item No	Checklist item	Supplement for MARE	Reported on page #
OTHER INFORMATION				
Registration	23	Registration number and name of trial registry		_____
Protocol	24	Where the full trial protocol can be accessed, if available		_____
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		_____

* Present the number as a total and with detail by gestational age in days in reference to completed weeks (e.g., ≤49 days, 50–56 days, 57–63 days, 64–70 days). Note that gestations less than 49 days can be further differentiated at the discretion of the investigators.

randomized trials) and STROBE guidelines (for prospective and retrospective cohort studies), referred to as *MARE*, *MARE-C* and *MARE-S*, respectively. The goals of these guidelines align with the CROWN and COMET initiatives to promote core outcome data sets [10,11].

2. The MARE supplement

The MARE supplement consists of 14 additional items that clarify the existing CONSORT (MARE-C, Table 1) and STROBE (MARE-S, Table 2) guidelines for early medical abortion trials. The aims of the statement are primarily to ensure standardized reporting of the regimen used, number of women treated, number who had follow-up (outcome) data available and efficacy outcomes by gestational age. Reporting outcomes in a standard manner will ensure that data are available for better synthesis into evidence-based guidelines. These guidelines will be helpful in designing prospective early medical abortion studies to ensure that the data can be reported systematically. Although retrospective studies may not have enough information to always meet the recommendations, authors can use the guidelines to identify limitations of their dataset. The MARE supplements are not intended to be an independent assessment of the quality of the clinical trial.

To facilitate searching through publication and clinical trial databases for studies to include in outcome data sets, we recommend standardization of key words to be included with each manuscript or trial registration. These words should include, at a minimum, the term *medical abortion* (or "medication abortion"), each of the agents used for treatment (e.g., mifepristone, misoprostol) and the route of the prostaglandin analog (e.g., oral, vaginal, buccal, sublingual).

3. Endorsement

The Society of Family Planning, an academic society dedicated to improving sexual and reproductive health, endorses these guidelines. We hope that abortion researchers as well as funders of abortion research will support the MARE supplements to CONSORT (MARE-C) and STROBE (MARE-S). We invite the editors of women's health scientific journals to include the MARE supplements in author guidelines. The supplements will be maintained and updated by the Society of Family Planning.

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Table 2
The STROBE supplement checklist for early MARE (MARE-S)

Section/Topic	Item No	Checklist item	Supplement for MARE	Reported on page #
TITLE AND ABSTRACT				
Title	1a	Indicate the study's design with a commonly used term in the title or the abstract		
Abstract	1b	Provide in the abstract an informative and balanced summary of what was done and what was found		
INTRODUCTION				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		
Objectives	3	State specific objectives, including any pre-specified hypotheses		
METHODS				
Study design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	6–1 Detail the range of gestational age for participants determined a priori to be included in the research, including a lower limit when applicable.	
			6–2 Explain the methods used to determine gestational age (e.g., physical examination, last menstrual period, ultrasonography). If ultrasonography is used, detail the type (vaginal and/or abdominal) and consider describing the criteria used for determination of gestational age.	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	7–1 Exposure: Detail the medications used, including dose(s) and route(s) of administration. If more than one medication is used, state the planned time interval between medications, preferably in hours.	
			7–2 Outcome: Define successful medical abortion (should most commonly be considered as successful expulsion of the intrauterine pregnancy without need for surgical intervention).	
			7–3 Outcome: Define the types of medical abortion failure (e.g., ongoing pregnancy, incomplete abortion, participant symptoms). Continuing pregnancy should be defined as a viable pregnancy following treatment (to be differentiated from a non-viable [i.e., retained gestational sac]).	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.	8–1 Assessment: Explain the follow-up assessments used to determine outcome (e.g., urine pregnancy test, serum pregnancy test, ultrasonography, physical exam, symptoms checklist).	
			8–2 Assessment: Explain the length of time planned to follow participants for determination of outcomes.	
Bias	9	Describe any efforts to address potential sources of bias		
Study size	10	Explain how the study size was arrived at		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.		
Statistical methods	12a	Describe all statistical methods, including those used to control for confounding		
	12b	Describe any methods used to examine subgroups and interactions		
	12c	Explain how missing data were addressed		
	12d	If applicable, explain how loss to follow-up was addressed		
	12e	Describe any sensitivity analyses		

(continued on next page)

Table 2 (*continued*)

Section/Topic	Item No	Checklist item	Supplement for MARE	Reported on page #
RESULTS				
Participants	13a*	Report numbers of individuals at each stage of study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed)	13a-1 Report the number of participants who started medical abortion treatment and the number who did not complete any follow-up for each cohort and by gestational age.†	_____
			13a-2 Report the number of participants used in the denominator for outcome evaluation for each cohort and by gestational age†, which most commonly will be the number of women with any follow-up.†	_____
			13a-3 Include a description of the number of women who used the drug(s) as planned in the protocol (treatment adherence).	_____
			13a-4 When more than one drug is used (e.g. mifepristone and a prostaglandin analog), the actual time interval between the agents should be reported, preferably in hours.	_____
	13b*	Give reasons for non-participation at each stage		_____
	13c*	Consider use of a flow diagram		_____
Descriptive data	14a*	Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders		_____
	14b*	Indicate number of participants with missing data for each variable of interest		_____
	14c*	Summarize follow-up time (average and total amount)		_____
Outcome data	15*	Report numbers of outcome events or summary measures over time		_____
Main results	16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included.	16a-1 Present treatment success for each cohort and by gestational age.†	_____
			16a-2 Present continuing pregnancies for each cohort and by gestational age.†	_____
			16a-3 Present reasons for surgical intervention other than continuing pregnancy for each cohort and by gestational age.†	_____
	16b	Report category boundaries when continuous variables were categorized		_____
	16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		_____
Other analyses	17	Report other analyses done (e.g., analyses of subgroups and interactions, and sensitivity analyses)		_____
DISCUSSION				
Key results	18	Summarize key results with reference to study objectives		_____
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.		_____
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		_____
Generalizability	21	Discuss the generalizability (external validity) of the study results		_____
OTHER INFORMATION				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		_____

* Give information separately, if applicable, for exposed and unexposed groups in cohort studies.

† Present the number as a total and with detail by gestational age in days in reference to completed weeks (e.g., ≤ 49 days, 50–56 days, 57–63 days, 64–70 days). Note that gestations less than 49 days can be further differentiated at the discretion of the investigators.

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