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The obstetrical research landscape: a cross-sectional analysis of clinical trials from 2007-2020

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BACKGROUND: Obstetrical complications affect more than a third of women globally, but are underrepresented in clinical research. Little is known about the comprehensive obstetrical clinical trial landscape, how it compares with other fields, or factors associated with the successful completion of obstetrical trials.

OBJECTIVE: This study aimed to characterize obstetrical clinical trials registered on ClinicalTrials.gov with the primary objective of identifying features associated with early discontinuation and results reporting.

STUDY DESIGN: This is a cross-sectional study with descriptive, logistic regression and Cox regression analyses of clinical trials registered on ClinicalTrials.gov. Our primary exposure variables were trial focus (obstetrical or nonobstetrical) and trial funding (industry, United States government, or academic). We conducted additional exploratory analyses of other trial features including design, enrollment, and therapeutic focus. We examined the associations of exposure variables and other trial features with 2 primary outcomes: early discontinuation and results reporting.

RESULTS: We downloaded data for all studies (N=332,417) registered on ClinicalTrials.gov from October 1, 2007, to March 9, 2020, from the Aggregate Analysis of ClinicalTrials.gov database. We excluded studies with a noninterventional design (n=63,697) and those registered before October 1, 2007 (n=45,209). A total of 4276 obstetrical trials (1.9%) (ie, interventional studies) and 219,235 nonobstetric trials (98.1%) were compared. Among all trials, 2.8% of academic-funded trials, 1.9% of United States government–funded trials, and 0.4% of industry-funded trials focused on obstetrics. The quantity of obstetrical trials increased over time (10.8% annual growth rate). Compared with nonobstetrical trials, obstetrical trials had a greater risk of early discontinuation (adjusted hazard ratio, 1.40; 95% confidence interval, 1.21–1.62; $P<.0001$) and similar odds of results reporting (adjusted odds ratio, 0.89; 95% confidence interval, 0.72–1.10; $P=.19$). Among obstetrical trials funders after controlling for confounding variables, United States government–funded trials were at the lowest risk of early discontinuation (United States government, adjusted hazard ratio, 0.23; 95% confidence interval, 0.07–0.69; $P=.009$; industry reference; academic, adjusted hazard ratio, 1.04; 95% confidence interval, 0.62–1.74; $P=.88$). Academic-funded trials had the lowest odds of results reporting after controlling for confounding variables (academic institutions, adjusted odds ratio, 0.39; 95% confidence interval, 0.22–0.68; $P=.0009$; industry reference; United States government, adjusted odds ratio, 1.06; 95% confidence interval, 0.53–2.09; $P=.87$).

CONCLUSION: Obstetrical trials represent only 1.9% of all clinical trials in ClinicalTrials.gov and have comparatively poor completion. All stakeholders should commit to increasing the number of obstetrical trials and improving their completion and dissemination to ensure clinical research reflects the obstetrical burden of disease and advances maternal health.

Key words: ClinicalTrials.gov, industry, maternal-fetal medicine, maternal health, National Institutes of Health, obstetrical complications, obstetrical investigations, obstetrical morbidity, obstetrical studies, research funding

Introduction

Clinical trials represent the gold standard for advancing evidence-based medicine and clinical care.[1] ClinicalTrials.gov is one of the largest international databases of clinical trials, containing nearly half of all registered trials.[2] Since 2007, the United States federal law has required that most phase 2 to 4 intervention studies register in ClinicalTrials.gov.[3]

EDITOR'S CHOICE

Obstetrical complications affect nearly a third of women in high-income countries and a greater proportion of women in low-income countries.[4] Despite the perinatal burden of disease, proportionally few clinical trials focus on complications of pregnancy, and pregnant women are often excluded from clinical trials that evaluate therapies used to treat chronic conditions in pregnant women.[5] To address the paucity of obstetrical studies, the National Institutes of Health put forth guidelines to safely include pregnant women in clinical trials and recommended trial breadth capture the spectrum of pharmaceuticals commonly taken during pregnancy.[6] In addition, the World Health Organization,[7] the Institute of Medicine,[8] the Centers for Disease Control and Prevention,[9] and the American College of Obstetricians and Gynecologists[10] called for increased obstetrical clinical trials and for the quantity of obstetrical trials to better match the obstetrical burden of disease.

Despite these initiatives, the landscape and key drivers of obstetrical clinical trial success remain poorly understood. Previous studies describing obstetrical clinical trials examined only small sample sizes or short time frames, and none included multivariable associative

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AJOG MFM at a Glance

Why was this study conducted?

This study aimed to characterize obstetrical clinical trials and determine which trial features are associated with trial completion and results reporting.

Key findings

Less than 2% of clinical trials registered to ClinicalTrials.gov between 2007 and 2020 focused on obstetrics. Obstetrical trials were at a greater risk of early discontinuation than nonobstetrical trials. Among obstetrical trials, United States government–funded trials were least likely to be discontinued early and academic institution–funded trials had the lowest odds of results reporting compared with other funders.

What does this add to what is known?

This study presents a comparison of obstetrical and nonobstetrical trials that includes funding sources and trial characteristics, novel assessments of temporal trends only possible with a large sample size and greater time period, and a unique examination of associations between obstetrical trial funding and the likelihood of early discontinuation and results reporting, while controlling for confounding variables.

analyses.[5,11–13] A comprehensive understanding of obstetrical clinical trials to date presents a first step toward determining how to improve and expand the evidence base. In view of the importance of clinical trials informing evidence-based care, we sought to characterize and analyze key features of obstetrical studies registered on ClinicalTrials.gov and to identify factors associated with early trial discontinuation and results reporting.

Materials and Methods

Data source

We downloaded data for all studies submitted to ClinicalTrials.gov before March 9, 2020, from the Aggregate Analysis of ClinicalTrials.gov (AACT) database.[14] We selected studies after October 1, 2007, to align with the Food and Drug Administration Amendments Act, which mandated the registration of most United States phase 2 to 4 intervention studies in ClinicalTrials.gov.[15] After the implementation of the Food and Drug Administration Amendments Act, ClinicalTrials.gov captured a more representative sample of the entire clinical trial landscape, and for many years after, it was the largest database of clinical trials globally.[16] We included all registered studies with an interventional study design (ie, clinical trials). We excluded studies registered before October 1, 2007, and those with an observational design (ie, not clinical trials). The University Institutional Review Board exempted our study from review because it only involved publicly available data without personal health information or human subjects.

Definitions

Obstetrical and nonobstetrical trials

To identify potential obstetrical trials, we followed a published protocol to identify Medical Subject Heading and disease terms relevant to obstetrical trials.[17,18] The protocol for extraction and categorization was set a priori (detailed definitions and labeling methods described in the Appendix). These terms were then used to extract data on all trials relevant to obstetrics from the AACT database.[14] Obstetrical trials were manually reviewed, verified, and categorized to one or multiple therapeutic focus categories as follows: cesarean delivery; nutritional status in pregnancy; labor anesthesia and analgesia; infections in pregnancy, labor, and the puerperium; fetal focused; threatened early delivery; mental and behavioral disorder; diabetes mellitus in pregnancy; bleeding and hemorrhage; labor augmentation and induction; hypertensive disorders of pregnancy; breastfeeding; pregnancy loss; obstetrical trauma; thromboembolic disease of pregnancy; vomiting in pregnancy; and other. Nonobstetrical trials were defined as all trials in the AACT database within the same time frame and without content relevant to obstetrics. The 2 first authors and the 7 trained researchers who labeled all trials demonstrated more than 90% agreement on a training set of more than 200 trials. To verify data, the first author randomly selected more than 10% of all labeled trials for concordance with the protocol. The first authors adjudicated all discrepancies in labeling.

For analysis, each therapeutic focus was treated as a binary variable with 2 categories: (1) trials labeled with the therapeutic focus and (2) all other trials that were not labeled with the therapeutic focus.

Exposures and outcomes

Our primary exposure variables were trial focus (obstetrical or nonobstetrical) and trial funding (industry, United States government, or academic). We conducted additional exploratory analyses of other trial features including characteristics, design, enrollment, and therapeutic focus. Obstetrical trials were compared with nonobstetrical trials in terms of funding source and other trial features. Obstetrical trial features were also compared by trial funder.

We examined the associations of the exposure variables and other trial features with 2 primary outcomes: early discontinuation and results reporting within 3 years of trial completion. "Early discontinuation" was defined as a trial stopped early with the status "Terminated" or "Suspended." In analysis of early discontinuation, we excluded trials documented as having a duration of <1 day (2.1%), trials with the status "Withdrawn" (defined as those terminating before the enrollment of participants [2.8%]), and trials without a verified status (13.2%).[19] Only trials completed by March 9, 2017, were included in the analysis of results reporting to align with federal mandates for delayed submission of results within 3 years of trial completion.[20]

Trial features

We categorized 12 trial features for comparison and exposure analysis: (1) funding, (2) primary purpose, (3) phase, (4) number of arms, (5) enrollment, (6) year of trial registration, (7) blinding, (8) randomization, (9) oversight by a data safety monitoring committee, (10) location, (11) number of sites, and (12) study status.[17]

"Enrollment" included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment).

We classified "funding" consistently with previous studies based on the trial sponsor and collaborating agencies.[17,18] If industry was a trial's sponsor or a collaborator, the trial was classified as "industry." Among remaining trials, if the United States government (ie, National Institutes of Health or another United States government agency) was the sponsor or a collaborator, the trial was classified as "United States government." The remaining trials were categorized "academic" after a random sample analysis of 2500 remaining funders identified that 90.1% (99% confidence interval [CI], 88.56–91.64) of these funding sources were academic institutions as defined with United States legal code.[21,22]

"Location" was classified based on the World Bank definitions of high-, middle-, and low-income countries.[23] Trials with at least 1 site in a high-income country were considered high income, and those in low- and middle-income countries were considered low and middle income.

Analysis

We summarized data with descriptive statistics including frequencies, percentages, and 2-sided Pearson chi-square tests. We analyzed change over time—independence and significance with annual growth rates and post hoc Mann-Kendall tests, respectively.[24] Only years with a completed 12-month cycle were included in growth analyses (2008–2019).

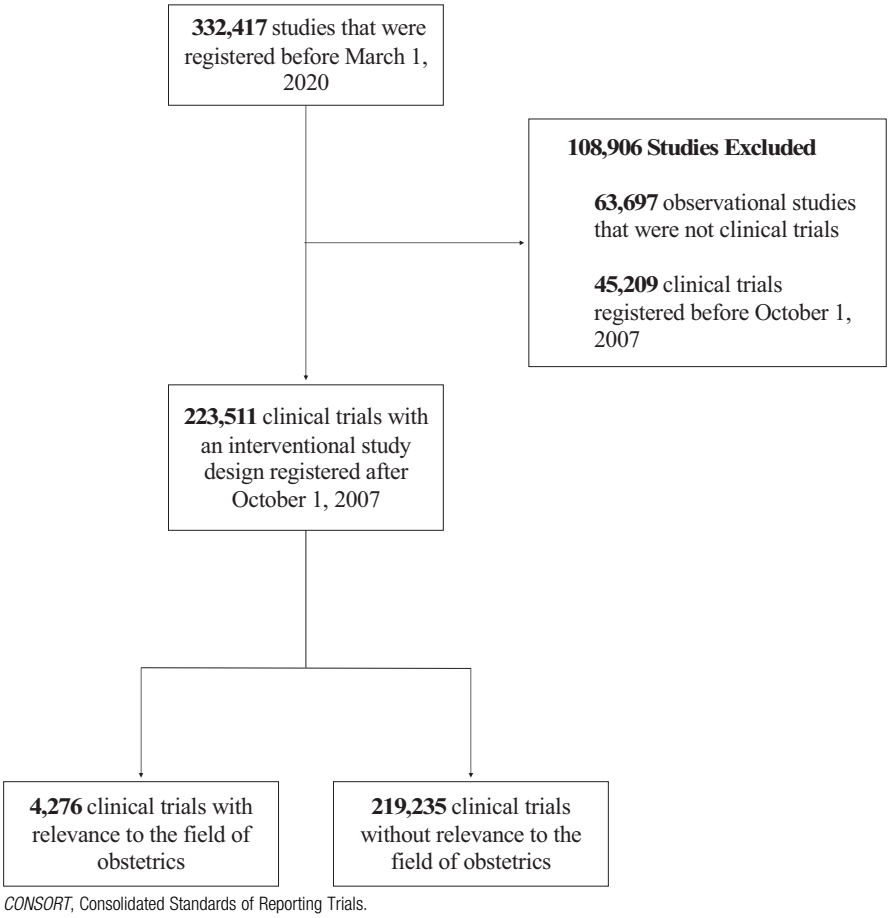
We conducted univariable and multivariable analyses with Cox proportional hazard models for early discontinuation and logistic regression for results reporting resulting in adjusted hazard ratios (aHRs) and adjusted odds ratios (aORs). Although we created Kaplan-Meier curves for both outcomes, the analysis of results reporting used only a logistic model. Cox models for early discontinuation use a time variable consistent with the duration of each trial from initiation to either discontinuation (event) or if ongoing the data download date. Log-rank tests were used to verify the independence of the Kaplan-Meier curves. All 12 trial features listed earlier, except for the trial feature under investigation, were treated as confounding variables in multivariable analysis.

All analyses were 2 sided with statistical significance at the α=.05 level. Analyses were performed using the R statistical programming language, version 3.5.0 (The R Foundation, https://www.r-project.org/).

Missing data

Multiple imputation analysis and multiple imputation by chained equations were conducted for all missing data in multivariable analysis.[25,26] We generated 20 imputed datasets and modeled continuous data using Bayesian linear regression, binary data with Bayesian logistic regression, and categorical data with Bayesian polytomous regression, all with analytical variables as covariables. Parameters of interest were estimated separately in each imputed dataset and subsequently pooled using Rubin's rules.[27] We present the imputed outcomes in results.

FIGURE 1
CONSORT diagram of clinical trials included in the analysis



CONSORT, Consolidated Standards of Reporting Trials.

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

Results

Trial population

A total of 332,417 studies were registered in ClinicalTrials.gov on March 9, 2020; 108,906 studies were excluded because they were registered before 2007 (n=45,209) or had a noninterventional study design (n=63,697) (Figure 1). Of the trials included, 1.9% (n=4276) were obstetrical trials, with more than 3.4 million estimated participants, and 98.1% (n=219,235) were nonobstetrical comparison trials.

Obstetrical trials compared with nonobstetrical trials

Funding

The funding sources of obstetrical trials differed from nonobstetrical trials, with the vast majority of obstetrical clinical trials funded by academic institutions (85.5%) followed by the United States government (7.7%) and industry (6.8%) (Figure 2; Supplemental Table 1). In contrast, a large proportion of nonobstetrical trials were funded by both academic institutions (57.1%) and industry (35.0%), with a smaller proportion funded by the United States government (7.9%). Among all trials, obstetrics was the focus in 2.8% of academic-funded trials, 1.9% of United States government–funded trials, and 0.4% of industry-funded trials.

Other trial characteristics

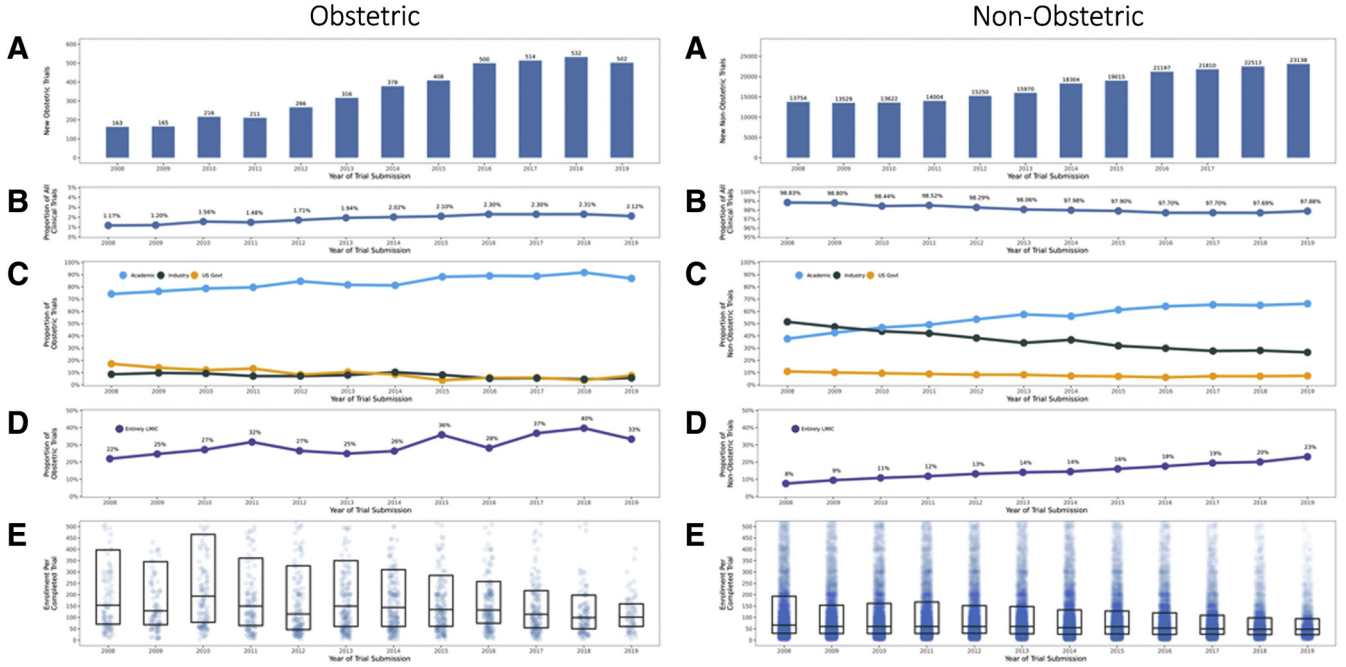
Obstetrical trials focused on prevention more frequently (31.5% vs 10.2%) and on treatment less frequently than nonobstetrical trials (39.3% vs 64.0%) (Supplemental Table 1). Obstetrical trials had more participants per trial (enrollment of >100, 61.5% vs 35.4%) and had more frequent blinding, randomization, and reporting to a data safety monitoring committee. A greater proportion of obstetrical trials occurred exclusively in low- and middle-income countries (27.5%) than nonobstetrical trials (13.9%). The quantity of obstetrical trials increased at a greater annual growth rate than nonobstetrical trials (obstetrical 10.8% vs nonobstetrical 4.8%) (Supplemental Table 2).

Obstetrical trial characteristics

Funding

Within obstetrical trials, compared with other sources of funding, those with United States government funding had more randomization, increased enrollment (>100), and more oversight by a data safety monitoring committee (Table 1). In contrast, a greater proportion of obstetrical trials with industry funding

FIGURE 2
Characteristics of obstetrical and nonobstetrical trials over time



A, Number of trials. **B,** Percentage of total trials. **C,** Percentage of trials within obstetrical and nonobstetrical trials funded by industry, the United States government, or academics. Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials. **D,** Percentage of trials within obstetrical trials and nonobstetrical trials in only low- and middle-income countries. **E,** Density plot of trial enrollment; each dot represents 1 trial. Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment).

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

TABLE 1
Characteristics of obstetrical trials by funding[a,b]

Trial feature	Industry	Academic	United States government	Chi^2 *P* value
Total	290 (6.8)	3655 (85.6)	331 (7.7)	
Primary purpose				
Treatment	116 (40.0)	1467 (40.1)	98 (29.6)	.0002
Basic science	5 (1.7)	84 (2.3)	17 (5.1)	
Prevention	92 (31.7)	1119 (30.6)	134 (40.5)	
Other[c]	67 (23.1)	894 (24.5)	76 (23.0)	
Missing	10 (3.4)	91 (2.5)	6 (1.8)	
Phase				
Not Applicable[d]	127 (43.8)	2455 (67.2)	223 (67.4)	<.0001
Phase 1	13 (4.5)	107 (2.9)	16 (4.8)	
Phase 1/2—2	46 (15.9)	221 (6.0)	34 (10.3)	
Phase 2/3—3	58 (20.0)	414 (11.3)	35 (10.6)	
Phase 4	46 (15.9)	458 (12.5)	23 (6.9)	
Enrollment[e]				
0—9	25 (8.6)	169 (4.6)	10 (3.0)	<.0001
10—49	57 (19.7)	545 (14.9)	39 (11.8)	
50—99	38 (13.1)	698 (19.1)	53 (16.0)	
100—499	115 (39.7)	1655 (45.3)	140 (42.3)	
500—999	24 (8.3)	237 (6.5)	34 (10.3)	
>999	30 (10.3)	337 (9.2)	55 (16.6)	
Missing	1 (0.3)	14 (0.4)	0	
Blinding				
None	166 (57.2)	1926 (52.7)	174 (52.6)	<.0001
Single	31 (10.7)	947 (25.9)	100 (30.2)	
Double	93 (32.1)	773 (21.1)	56 (16.9)	
Missing	0	9 (0.2)	1 (0.3)	
Randomization				
Nonrandomized	80 (27.6)	706 (19.3)	36 (10.9)	<.0001
Randomized	207 (71.4)	2918 (79.8)	295 (89.1)	
Missing	3 (1.0)	31 (0.8)	0	
Oversight by a data safety monitoring committee				
No	155 (53.4)	1976 (54.1)	138 (41.7)	<.0001
Yes	120 (41.4)	1341 (36.7)	174 (52.6)	
Missing	15 (5.2)	338 (9.2)	19 (5.7)	
Location				
High-income countries	210 (72.4)	2125 (58.1)	222 (67.1)	<.0001
Low- and middle-income countries only	47 (16.2)	1048 (28.7)	79 (23.9)	
Missing	33 (11.4)	482 (13.2)	30 (9.1)	
Therapeutic focus[f]				
Infection	55 (19.0)	283 (7.7)	100 (30.2)	<.0001

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

(continued)

TABLE 1
Characteristics of obstetrical trials by funding[a,b] *(continued)*

Trial feature	Industry	Academic	United States government	Chi^2 *P* value
Nutrition	40 (13.8)	458 (12.5)	55 (16.6)	.10
Fetal	27 (9.3)	378 (10.3)	17 (5.1)	.009
Early delivery	25 (8.6)	292 (8.0)	11 (3.3)	.002
Diabetes mellitus	22 (7.6)	266 (7.3)	19 (5.7)	.56
Mental health	21 (7.2)	267 (7.3)	66 (19.9)	<.0001
Cesarean delivery	19 (6.6)	659 (18.0)	8 (2.4)	<.0001
Labor Augmentation	19 (6.6)	235 (6.4)	3 (0.9)	.0002
Hemorrhage	19 (6.6)	281 (7.7)	5 (1.5)	.0001
Hypertension	13 (4.5)	229 (6.3)	12 (3.6)	.08
Breastfeeding	10 (3.4)	158 (4.3)	29 (8.8)	.0006
Anesthesia	10 (3.4)	501 (13.7)	4 (1.2)	<.0001
Trauma	7 (2.4)	85 (2.3)	3 (0.9)	.24
Pregnancy loss	6 (2.1)	139 (3.8)	4 (1.2)	.02
Thromboembolic	3 (1.0)	21 (0.6)	0	.22
Vomiting	2 (0.7)	17 (0.5)	2 (0.6)	.83
Other	37 (12.8)	441 (12.1)	44 (13.3)	.77

Values are number (percentage) unless indicated otherwise.

[a] Percentages may not sum up to 100 because of rounding; [b] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials; [c] Other primary purposes include diagnostic, screening, supportive care, health services research, and other; [d] On ClinicalTrials.gov, "Not Applicable" is used to describe trials without Food and Drug Administration–defined phases, including trials of devices or behavioral interventions; [e] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment); [f] Trials could have >1 therapeutic focus. For analysis, each therapeutic focus was treated as a binary variable.

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

had lower enrollment (<100), no blinding, and no randomization.

Change over time

The total number of obstetrical trials doubled from 2007 to 2013 (n=1366) to 2014 to 2020 (n=2910) (Figure 2). The increase in obstetrical trials varied by funding source: academic-funded trials increased at nearly double the rate of industry-funded trials, and United States government–funded trials had no meaningful change (Supplemental Table 2).

Therapeutic focus

The plurality of obstetrical trials focused on cesarean delivery (16.0% of all obstetrical trials) (Supplemental Table 3) with most of these funded by academic institutions (Table 1). Infection was the most frequent therapeutic focus among both industry- (19.0%) and United States government–funded trials (30.2%). Obstetrical trauma, thrombosis, and vomiting were the least frequent therapeutic foci across all funders with the lowest enrollment (Supplemental Figure; Supplemental Table 3).

Early trial discontinuation

Obstetrical trials compared with nonobstetrical trials

Between 2007 and 2020, 47.5% of all obstetrical trials reached completion, representing more than 2.8 million participants (Supplemental Table 4). A total of 7.2% trials were discontinued early and 13.2% had missing or unknown study status. In contrast, 51.3% of nonobstetrical trials were completed, 8.8% were discontinued early, and 10.2% had missing or unknown study status. Compared with nonobstetrical trials, obstetrical trials had a greater adjusted risk of early discontinuation (aHR, 1.40; 95% CI, 1.21–1.62; *P*<.0001) (Table 2; unadjusted analysis results in Supplemental Table 5).

Obstetrical trials only

Among obstetrical trials, United States government–funded trials had the lowest adjusted risk of early discontinuation of any funding source (United States government, aHR, 0.23; 95% CI, 0.07–0.69; *P*=.009, industry reference; academic, aHR, 1.04; 95% CI, 0.62–1.74; *P*=.88, Figure 3). Randomized trials and trials in high-income countries had a greater adjusted hazard of early discontinuation than nonrandomized trials and trials exclusively in low- and middle-income countries, respectively (randomization, aHR, 2.00; 95% CI, 1.28–3.13; *P*=.002; location, aHR, 1.83; 95% CI, 1.05–3.21; *P*=.03). Trials with the therapeutic foci of either anesthesia or cesarean delivery showed a greater adjusted hazard of early

TABLE 2
Associations between trail features and early discontinuation in obstetrical clinical trials

Trial feature	Hazard ratio (95% confidence interval)	*P* value
All trials		
Nonobstetrical	Reference	
Obstetrical	1.40 (1.21–1.62)	<.0001
Obstetrical trials only		
Funding[a]		
Industry	Reference	
Academic	1.04 (0.62–1.74)	.88
United States government	0.23 (0.07–0.69)	.009
Primary purpose		
Treatment	Reference	
Basic science	0.58 (0.17–1.99)	.38
Prevention	0.95 (0.64–1.42)	.82
Other[b]	1.33 (0.87–2.03)	.19
Phase		
Phase 2/3–3	Reference	
Not Applicable[c]	0.54 (0.34–0.86)	.009
Phase 1	0.52 (0.25–1.09)	.08
Phase 1/2–2	0.64 (0.33–1.23)	.18
Phase 4	1.17 (0.67–2.04)	.15
Enrollment[d]		
100–499	Reference	
0–9	49.82 (30.10–82.47)	<.0001
10–49	6.29 (4.10–9.64)	<.0001
50–99	2.01 (1.20–3.36)	.007
500–999	0.72 (0.25–2.02)	.53
>999	0.79 (0.37–1.65)	.53
Blinding		
None	Reference	
Single	0.62 (0.40–0.96)	.03
Double	0.83 (0.54–1.26)	.37
Randomization		
Nonrandomized	Reference	
Randomized	2.00 (1.28–3.13)	.002
Oversight by a data safety monitoring committee		
No	Reference	
Yes	1.12 (0.82–1.54)	.47
Location		
Low- and middle-income country only	Reference	
High-income country	1.83 (1.05–3.21)	.03
Number of facilities		

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

(continued)

TABLE 2
Associations between trail features and early discontinuation in obstetrical clinical trials *(continued)*

Trial feature	Hazard ratio (95% confidence interval)	*P* value
1	Reference	
>2	1.35 (0.92–1.98)	.13
Therapeutic focus[e]		
All other trials	Reference	
Cesarean delivery	1.72 (1.03–2.87)	.04
Nutrition	1.04 (0.63–1.73)	.87
Anesthesia	1.86 (1.12–3.10)	.02
Infection	1.57 (0.95–2.62)	.08
Fetal	0.95 (0.59–1.51)	.81
Mental health	0.94 (0.52–1.70)	.84
Early delivery	1.08 (0.67–1.74)	.75
Diabetes mellitus	0.59 (0.33–1.06)	.08

[a] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials; [b] Other primary purposes include diagnostic, screening, supportive care, health services research, and other; [c] On ClinicalTrials.gov, "Not Applicable" is used to describe trials without Food and Drug Administration–defined phases, including trials of devices or behavioral interventions; [d] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment); [e] Trials could have >1 therapeutic focus. For analysis, each therapeutic focus was treated as a binary variable.

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

discontinuation than any other therapeutic foci.

Results reporting

Obstetrical trials compared with nonobstetrical trials

Obstetrical trials had similar adjusted odds of reporting results as nonobstetrical trials (aOR, 0.89; 95% CI, 0.72–1.10; *P*=.19) (unadjusted analysis results in Supplemental Table 6, adjusted analysis results in Supplemental Table 7).

Obstetrical trials only

By March 8, 2017, a total of 1411 obstetrical trials (102 industry, 138 United States government, and 1171 academic) had reached completion, but only 216 (15.3%) reported results to ClinicalTrials.gov by March 9, 2020 (Supplemental Tables 6 and 8).

Among obstetrical trials, academic-funded trials had the lowest adjusted odds of reporting results compared with other funders (academic, aOR, 0.39; 95% CI, 0.22–0.68; *P*=.0009; industry reference; United States government, aOR, 1.06; 95% CI, 0.53–2.09; *P*=.87) (Figure 4; Supplemental Table 5). Trials that focused on cesarean deliveries had the greatest adjusted odds of reporting results (aOR, 2.07; 95% CI, 1.29–3.34; *P*=.003) compared with other trial foci. Trials in high-income counties had greater results reporting than those exclusively in low- and middle-income countries (aOR, 2.13; 95% CI, 1.35–3.36; *P*=.001).

Comment

Principal findings

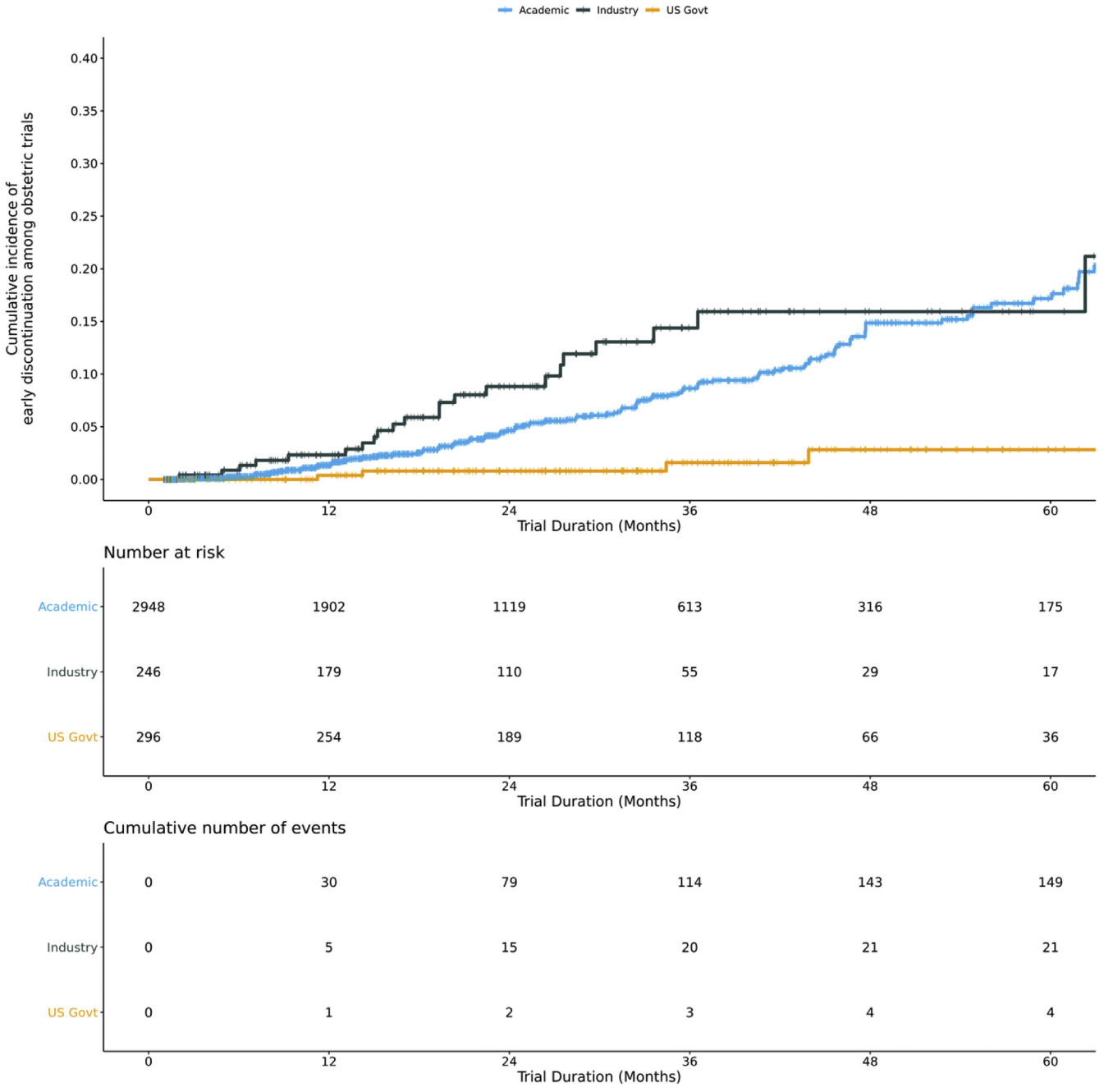
This study demonstrates that obstetrical clinical trials represent <2% of all clinical trials and, when initiated, are at a greater risk of early discontinuation than nonobstetrical trials. Although obstetrical trials report results at a similar rate to nonobstetrical, only 15.3% of completed obstetrical trials report results. Our temporal analysis shows limited improvement in obstetrical trial quantity, almost entirely driven by academic institutions.

Our study adds to previous investigations of obstetrical trials by suggesting the link among funding, metrics of trial quality, trial completion, and results reporting. We found that, among obstetrical trials, industry funds proportionally fewer large-scale trials, blinded trials, and randomized trials. In contrast, United States government–funded obstetrical trials are the most likely to meet the Consolidated Standards of Reporting Trials recommendations for trial quality[28] and to reach completion. When examining results reporting by funder, even after controlling for other variables, we identified that academic-funded trials are least likely to report results compared with other funders.

Results in context

Notably, 4 previous investigations have analyzed obstetrical trials in the ClinicalTrials.gov registry, all using a smaller sample of trials (n=325 trials[13] and n=5 trials[5]) or covering a shorter time span (2013–2014[11] and 2007–2012[12]). Although previous studies suggest that obstetrics is the focus of 6% of all trials[12] and 1%[5] to 16%[12] of industry-funded trials in ClinicalTrials.gov, our findings paint a bleaker picture; we found that only 1.9% of trials and 0.4% of industry-funded trials focus

FIGURE 3
Kaplan-Meier curves of early discontinuation by trial funder

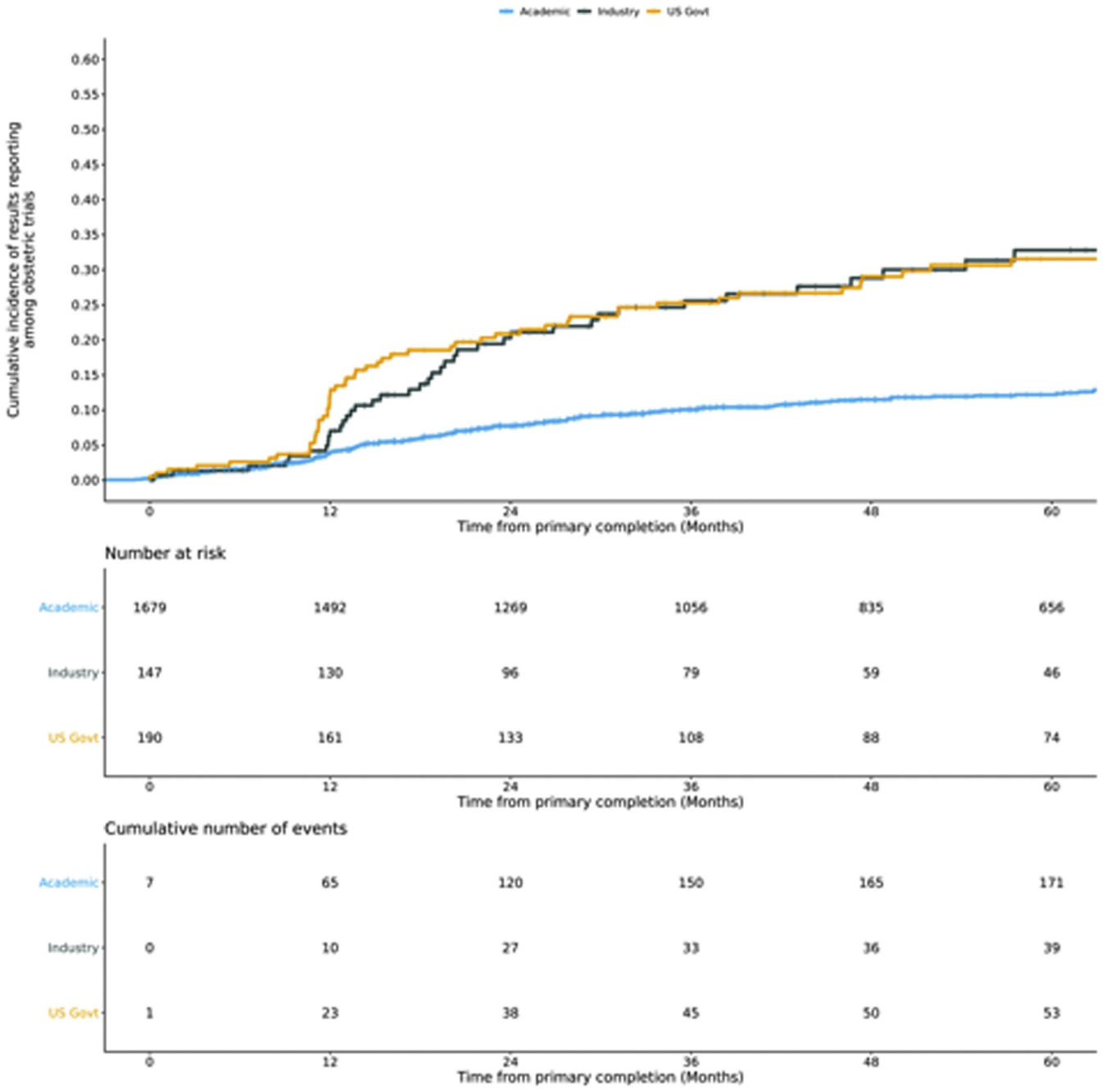


Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials. The log-rank *P* value for Kaplan-Meier curve was <.0001.

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

on obstetrics. Even with the inclusion of observational studies, the 6% estimate in Stockmann et al's[12] investigation still likely overrepresents obstetrical clinical trials, perhaps because their search query included neonatal terms and the study did not describe a manual review to remove trials unrelated to obstetrics after the query. Moreover, 3 of the previous obstetrical studies were limited to Federal and Drug Administration–approved trials,[13] pharmaceutical trials,[11] and phase 4 trials, respectively.[5] We included all obstetrical clinical trials

FIGURE 4
Kaplan-Meier curves of results reporting by trial funder



Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials.

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

between 2007 and 2020, but similarly found the number of obstetrical studies pales in comparison with that of other fields.

More studies were dedicated to oncology (8992), cardiology (3437), and mental health between 2007 and 2010 (3695)[29] than those dedicated to obstetrics in the decade after 2007 (3166). The paucity of obstetrical studies carries implications in the changing international health ecosystem. One recent

study found that only 1.7% of coronavirus disease 2019 research pertains to pregnancy.[30] Our findings suggest the limited number of obstetrical trials may correlate to the dearth of industry funding in obstetrics. Previous investigations have indicated that industry may forgo obstetrical trials owing to inadequate pipelines for obstetrical drug and device development,[31] regulatory and financial prioritization of participant homogeneity,[32] and avoidance of potential maternal and fetal liability.[33] This is an important delineation, because industry is one of the most significant contributors to production, marketing, and distribution of new therapies.[34] Furthermore, this deficit may have untoward implications for the development of pharmaceuticals and treatments specific for obstetrical conditions.

Clinical implications

Despite calls by leading experts and international organizations to increase obstetrical clinical trials,[7–10,35] the relative shortage in obstetrical clinical trials remains an urgent issue. Other studies have explored the multifaceted etiology of obstetrical trial scarcity including historical precedents, ethical quandaries, participant, funder and institutional review board reluctance, and risk assessment.[6,8,36,37] A recent report recommended increased funding from the National Institutes of Health specifically as a means to expand obstetrical and gynecologic research and improve women's health outcomes.[38] Obstetrical clinical research represents a key component of the multifaceted efforts needed to decrease the maternal burden of disease and advance treatments for obstetrical conditions.[4,35] The progress of the field warrants and partially depends on a greater commitment of resources and funding by all clinical trial sponsors.

In addition to increasing the number of obstetrical clinical trials, improvement in obstetrical trial completion and dissemination is important. We found that United States government–funded trials more consistently meet quality metrics (eg, sample size, randomization, blinding, and oversight by a data safety monitoring committee)[28] and more frequently reach completion than academic or industry trials. The quality and success of United States government–funded obstetrical trials may speak to the potential role of increased regulation and present a model for increasing obstetrical trials completion.

The low results reporting, particularly in academic-funded trials, may be a reflection of relatively limited resources in academia. Although federal statues require many clinical trials to report their results within one year with the option to delay for 2 years,[20] the parameters of the statutes have evolved over the past decade and barriers exist to consistent results reporting.[15,39–41] Stockmann et al[12] identified that for obstetrical trials, ClinicalTrials.gov provides the most complete repository for trial results, which is more comprehensive than peer-reviewed publications. Trial results and their implications take on a greater nuance in pregnancy trials where interventions may affect both maternal and fetal health.[42] A lack of results can bias the literature, squander limited resources, and hinder medical innovation. Greater results reporting within obstetrical trials continues to be a relevant goal with implications for all expecting parents.

Strengths and limitations

Our analysis uniquely compares obstetrical and nonobstetrical trials and trial features among different funders. This comparison allows for the extrapolation of factors that may contribute to the low number of obstetrical trials and the increased risk of early discontinuation among obstetrical trials. We present novel assessments of temporal trends only possible with a large sample size and greater time period. This study examines the associations between obstetrical trial funding and early discontinuation and results reporting while controlling for confounding variables. Our multivariable approach clarifies which trial features are most important when considering mechanisms to improve obstetrical clinical trial completion and dissemination.

Our study is not without limitations. First, the ClinicalTrials.gov registry represents only a sample of all global clinical trials.[15] However, 1 study found that ClinicalTrials.gov contains the greatest number of obstetrical trials compared with other databases.[11] Second, because this analysis involves multiple testing, it is possible that the strength of association seen for some trial features may be the result of chance. Finally, the limitations of ClinicalTrials.gov have been described in other studies and apply to this analysis. These include changes to the database over time,[40] nuances of recruitment description and progress,[12] the inability to verify the validity of all trial data,[18] and the limited trial features and descriptions available for analysis.

Research implications

We characterize the obstetrical clinical trial landscape and trial features associated with early discontinuation and results reporting. A more granular view of the research by disease category and analyses comparing trial quantity with burden of disease could highlight areas for increased clinical trial focus. In addition, manual reviews of trial discontinuation reasons could identify why trials in obstetrics discontinue early.

Conclusions

The obstetrical clinical trial portfolio remains sparse but has shown growth over time. Increased industry investment in obstetrical trials may present an important step toward expanding available obstetrical therapies. All stakeholders must commit to improving obstetrical clinical trial completion rates and results dissemination to ensure trial findings advance the maternal health evidence base. Clinical trial research—in conjunction with health system strengthening and effective national policies—could decrease maternal morbidity and mortality.[4] Improvement in obstetrical outcomes depends, in part, on research investments that bridge the gap between the breadth of obstetrical disease and the quantity, quality, and

dissemination of obstetrical clinical trials. ■

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Appendix

Obstetrical therapeutic focus and disease category definitions and subgroups

A total of 8 researchers were trained with respect to the obstetrical therapeutic focus categorization system. Collectively, they manually reviewed all trials including titles, abstracts, and detailed descriptions to verify and categorize obstetrical trials. Disagreements and inconsistencies were adjudicated by the lead authors (J.R.S. and B.T.W.).

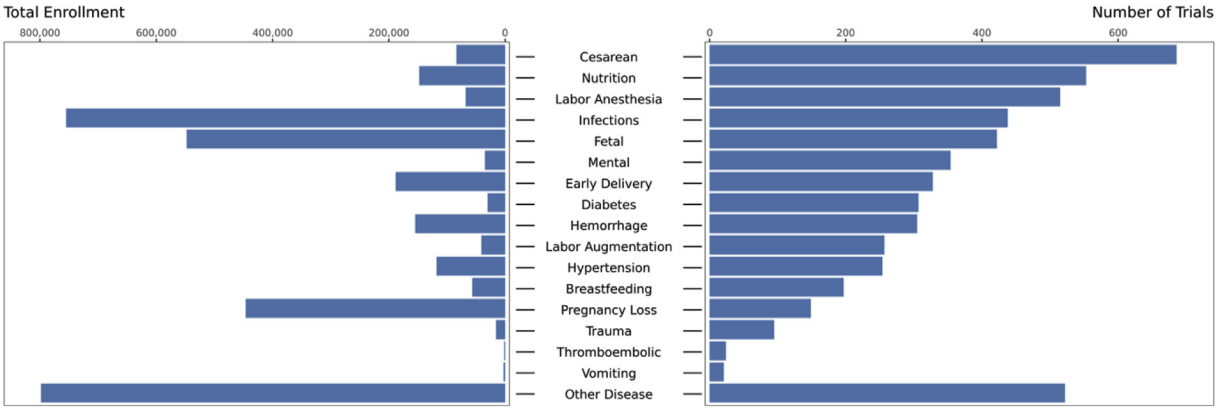
For analysis, each therapeutic focus was treated as a binary variable with 2 categories: (1) trials labeled with the therapeutic focus and (2) all other trials that were not labeled with the therapeutic focus (eg, [1] trials with the label "pregnancy loss," [2] trials without the label "pregnancy loss"). The reference for multivariate analysis of associations of therapeutic foci with trial outcomes was (2) all other trials that were not labeled with the therapeutic focus. Trials in the reference consequently varied among therapeutic foci.

The labels listed below were used to categorize the therapeutic foci of different obstetrical trials:

1. Cesarean delivery: All trials focused on cesarean delivery interventions or conducted only in patients receiving cesarean deliveries
2. Nutritional status in pregnancy: Trials that focused on obesity, malnutrition, mineral deficiencies, and/or amino acid deficiencies
3. Labor anesthesia and analgesia: Trials that focused on complications of anesthesia during pregnancy or after delivery, including pulmonary, cardiac, and central nervous system complications; toxic reaction to local anesthesia; spinal and epidural anesthesia—induced complications, including headache; and/or failed or difficult intubation
4. Infections in pregnancy, labor, and the puerperium: Trials that focused on chorioamnionitis; infections of genital and urinary tracts; sexually transmitted infections and pregnancy; viral hepatitis, HIV, and other viral infection; protozoal diseases; breast infections; pneumonia; tuberculosis; infection of the obstetrical surgical wound; fever of unknown origin; and/or sepsis
5. Fetal focused: Trials that focused on prenatal genetic screening, preimplantation genetic diagnosis, nonstress testing, intrapartum fetal heart rate monitoring, fetal (not neonatal) abnormalities, multiple gestation, polyhydramnios, oligohydramnios, hydrops, macrosomia, intrauterine growth restriction, and/or malpresentation
6. Threatened early delivery: Trials that focused on preterm labor, false labor, cervical insufficiency, and/or premature rupture of membranes
7. Mental and behavioral disorders: Trials that focused on postpartum mood disturbance or blues and/or postpartum depression or psychosis
8. Diabetes mellitus in pregnancy: Trials that focused on preexisting diabetes mellitus complicating pregnancy; and/or gestational diabetes
9. Bleeding and hemorrhage: Trials that focused on hemorrhage and spotting in early pregnancy; antepartum, intrapartum, and postpartum hemorrhage; placenta previa; placental abruption; placenta accreta, increta, and percreta; and/or postpartum uterine atony
10. Labor augmentation and induction: Trials that focused on postdates pregnancy, cervical ripening, induction of labor, and/or prolonged labor
11. Hypertensive disorders of pregnancy: Trials that focused on preexisting hypertension complicating the pregnancy, edema and proteinuria, pregnancy-induced hypertension, and/or preeclampsia and eclampsia
12. Breastfeeding: Trials that focused on breastfeeding, nipple pain/trauma, nipple infection, duct pathology, mastitis, breast abscess, and galactocele and hypogalactia
13. Pregnancy loss: Trials that focused on early pregnancy loss, ectopic pregnancy, spontaneous abortion, and/or fetal reduction
14. Obstetrical trauma: Trials that focused on perineal, high vaginal, or cervical laceration; uterine rupture; postpartum uterine inversion; obstetrical damage from instruments; obstetrical injury to pelvic organs; and/or pelvic hematoma
15. Thromboembolic disease of pregnancy: Trials that focused on deep vein thrombosis, amniotic fluid embolism, pyemic and septic embolism, and/or other obstetrical embolism (excluding cerebrovascular disease)
16. Vomiting in pregnancy: Trials that focused on excessive vomiting, hyperemesis gravidarum, late vomiting of pregnancy, and/or morning sickness
17. Other: Trials that focused on cerebrovascular disease (cerebral venous thrombosis, subarachnoid hemorrhage, and/or stroke), noninfectious liver disease in pregnancy (liver and biliary tract disorders, cholestasis of pregnancy, and/or acute fatty liver of pregnancy), and noninfectious renal disease in pregnancy (postpartum acute kidney failure, hepatorenal syndrome, kidney stones)

SUPPLEMENTAL FIGURE

Trial quantity and enrollment by therapeutic area of focus



Trials could have multiple therapeutic foci. Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment).

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SUPPLEMENTAL TABLE 1
Characteristics of obstetrical and nonobstetrical clinical trials[a]

Trial feature	Nonobstetrical	Obstetrical	Chi^2 *P* value
Total	219,235 (98.1)	4276 (1.9)	
Funding[b]			
Industry	76,768 (35.0)	290 (6.8)	<.0001
United States government	17,350 (7.9)	331 (7.7)	
Academic	125,117 (57.1)	3655 (85.5)	
Primary purpose			
Treatment	140,234 (64.0)	1681 (39.3)	<.0001
Basic science	12,154 (5.5)	106 (2.5)	
Prevention	22,394 (10.2)	1345 (31.5)	
Other[c]	37,961 (17.3)	1037 (24.3)	
Missing	6492 (3.0)	107 (2.5)	
Phase			
Not Applicable[d]	99,542 (45.4)	2805 (65.6)	<.0001
Phase 1	30,146 (13.8)	136 (3.2)	
Phase 1/2—2	42,144 (19.2)	301 (7.0)	
Phase 2/3—3	26,058 (11.9)	507 (11.9)	
Phase 4	21,345 (9.7)	527 (12.3)	
Enrollment[e]			
0—9	16,056 (7.3)	204 (4.8)	<.0001
10—49	78,930 (36.0)	641 (15.0)	
50—99	45,792 (20.9)	789 (18.5)	
100—499	61,257 (27.9)	1910 (44.7)	
500—999	8863 (4.0)	295 (6.9)	
>999	7628 (3.5)	422 (9.9)	
Missing	709 (0.3)	709 (0.3)	
Blinding			
None	124,461 (56.8)	2266 (53.0)	<.0001
Double	50,675 (23.1)	922 (21.6)	
Single	43,125 (19.7)	1078 (25.2)	
Missing	974 (0.4)	10 (0.2)	
Randomization			
Nonrandomized	74,065 (33.8)	822 (19.2)	<.0001
Randomized	142,302 (64.9)	3420 (80.0)	
Missing	2868 (1.3)	34 (0.8)	
Oversight by a data safety monitoring committee			
No	115,552 (52.7)	2269 (53.1)	<.0001
Yes	78,713 (35.9)	1635 (38.2)	
Missing	24,970 (11.4)	372 (8.7)	

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021. *(continued)*

SUPPLEMENTAL TABLE 1
Characteristics of obstetrical and nonobstetrical clinical trials[a] *(continued)*

Trial feature	Nonobstetrical	Obstetrical	Chi^2 *P* value
Location			
High-income countries	158,210 (72.2)	2557 (59.8)	<.0001
Low- and middle-income countries only	30,428 (13.9)	1174 (27.5)	
Missing	30,597 (14.0)	545 (12.7)	

Values are number (percentage) unless indicated otherwise.

[a] Percentages may not sum up to 100 because of rounding; [b] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials; [c] Other primary purposes include diagnostic, screening, supportive care, health services research, and other; [d] On ClinicalTrials.gov, "Not Applicable" is used to describe trials without Food and Drug Administration—defined phases, including trials of devices or behavioral interventions; [e] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment).

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SUPPLEMENTAL TABLE 2
Yearly growth statistics for obstetrical trials

Variable	Annual growth rate	Annual growth rate Mann-Kendall *P* value	Relative annual growth rate[a]	Relative annual growth rate Mann-Kendall *P* value
Obstetrical trials	10.8%	<.0001		
Nonobstetrical Trials	4.8%	<.0001		
Funding[b]				
United States government	2.8%	.49	−7.2%	.003
Industry	6.5%	.02	−3.8%	.05
Academic	12.4%	<.0001	1.4%	.0007
Study location				
High-income countries	7.9%	.0005	−1.4%	.007

[a] The relative annual growth rate (the change in percent) compares the relative growth of subcategories within a single category. It measures the change in the proportion of trials within that subcategory as a function of all trials in the category; [b] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials.

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SUPPLEMENTAL TABLE 3
Trial quantity and enrollment by therapeutic area of focus

Therapeutic area of focus[a]	Trials		Enrollment[b]	
Cesarean delivery	686	(16.0)	83,394	(2.4)
Nutrition	553	(12.9)	147,584	(4.2)
Other disease	522	(12.2)	798,361	(22.9)
Labor anesthesia	515	(12.0)	67,789	(1.9)
Infections	438	(10.2)	755,241	(21.6)
Fetal indications	422	(9.9)	547,647	(15.7)
Mental health	354	(8.3)	34,820	(1.0)
Early delivery	328	(7.7)	188,101	(5.4)
Diabetes mellitus	307	(7.2)	29,970	(0.9)
Hemorrhage	305	(7.1)	154,760	(4.4)
Labor Augmentation	257	(6.0)	40,946	(1.2)
Hypertension	254	(5.9)	118,076	(3.4)
Breastfeeding	197	(4.6)	56,389	(1.6)
Pregnancy loss	149	(3.5)	446,114	(12.8)
Trauma	95	(2.2)	15,585	(0.4)
Thromboembolic	24	(0.6)	1881	(0.1)
Vomiting	21	(0.5)	2658	(0.1)

Values are number (percentage) unless indicated otherwise.

[a] Trials could have multiple therapeutic areas of foci; [b] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment).
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SUPPLEMENTAL TABLE 4

Obstetrical trial study status and enrollment on March 9, 2020

Study status	Total trials	Total enrollment[a]
Completed		
Completed	2032	2,870,525
Ongoing		
Active, not recruiting	192	218,518
Enrolling by invitation	31	33,787
Not yet recruiting	249	234,939
Recruiting	899	693,661
Discontinued Early		
Suspended	10	1401
Terminated	181	30,369
Withdrawn	118	918
Unknown		
Unknown status	564	376,470

All definitions and terms as defined by the ClinicalTrials.gov glossary.[1]

[a] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment).

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SUPPLEMENTAL TABLE 5
Univariable analyses of association between trial between trail features and early discontinuation

Trail feature	Hazard ratio (95% confidence interval)	*P* value
Funding[a]		
Industry	Reference	
Academic	0.73 (0.45–1.18)	.20
United States government	0.12 (0.04–0.35)	<.001
Primary purpose		
Treatment	Reference	
Basic science	0.39 (0.12–1.30)	.12
Prevention	0.43 (0.29–0.62)	<.001
Other[b]	0.76 (0.51–1.13)	.17
Phase		
Phase 2/3–3	Reference	
Not Applicable[c]	0.95 (0.61–1.50)	.84
Phase 1	1.79 (0.83–3.88)	.14
Phase 1/2–2	1.13 (0.56–2.27)	.73
Phase 4	1.04 (0.58–1.88)	.90
Enrollment[d]		
100–499	Reference	
0–9	32.45 (20.75–50.75)	<.001
10–49	5.20 (3.39–7.99)	<.001
50–99	1.68 (0.97–2.93)	.07
500–999	0.72 (0.26–2.04)	.54
>999	0.81 (0.39–1.68)	.56
Year		
2007–2013	Reference	
2014–2020	1.17 (0.86–1.59)	.33
Blinding		
None	Reference	
Double	1.17 (0.83–1.66)	.37
Single	0.66 (0.43–1.00)	.053
Randomization		
Nonrandomized	Reference	
Randomized	0.87 (0.59–1.28)	.48
Oversight by a data safety monitoring committee		
No	Reference	
Yes	0.83 (0.61–1.13)	.24
Location		
Low- and middle-income countries only	Reference	
High-income countries	2.91 (1.68–5.04)	<.001

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

(continued)

SUPPLEMENTAL TABLE 5

Univariable analyses of association between trial between trail features and early discontinuation *(continued)*

Trail feature	Hazard ratio (95% confidence interval)	*P* value
Number of facilities		
1	Reference	
>2	0.92 (0.64–1.30)	.63
Therapeutic focus[e]		
All other therapeutic foci	Reference	
Cesarean delivery	1.51 (0.95–2.38)	.08
Nutrition	0.61 (0.37–0.99)	.046
Anesthesia	2.16 (1.42–3.29)	<.001
Infection	0.85 (0.52–1.41)	.53
Fetal	1.12 (0.72–1.75)	.61
Mental health	0.77 (0.43–1.38)	.38
Early delivery	1.47 (0.94–2.30)	.09
Diabetes mellitus	1.00 (0.59–1.71)	.99

[a] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency United States government trials include remaining trials with a United States government sponsor or collaborating agency; [b] Other primary purposes include diagnostic, screening, supportive care, health services research, and other; [c] On ClinicalTrials.gov, "Not Applicable" is used to describe trials without Food and Drug Administration–defined phases, including trials of devices or behavioral interventions; [d] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment); [e] Trials could have >1 therapeutic focus. For analysis, each therapeutic focus was treated as a binary variable.

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SUPPLEMENTAL TABLE 6

Univariable analyses of association between trial features and results reporting within 3 years of completion

Trail feature	Odds ratio (95% confidence interval)	*P* value
Funding[a]		
Industry	Reference	
Academic	0.48 (0.27–0.82)	.008
United States government	0.93 (0.47–1.83)	.83
Primary purpose		
Treatment	Reference	
Basic science	0.86 (0.33–2.26)	.76
Prevention	0.71 (0.48–1.07)	.10
Other[b]	0.71 (0.44–1.14)	.15
Phase		
Phase 2/3–3	Reference	
Not Applicable[c]	0.68 (0.40–1.16)	.16
Phase 1	0.81 (0.29–2.30)	.70
Phase 1/2–2	1.42 (0.70–2.86)	.33
Phase 4	1.23 (0.65–2.32)	.52
Enrollment[d]		
100–499	Reference	
10–49	1.13 (0.71–1.78)	.61
50–99	0.87 (0.54–1.38)	.55
500–999	0.70 (0.31–1.59)	.40
>999	0.44 (0.21–0.95)	.035
Year		
2007–2013	Reference	
2014–2020	1.22 (0.85–1.73)	.28
Blinding		
None	Reference	
Double	1.30 (0.85–2.00)	.22
Single	1.22 (0.80–1.86)	.36
Randomization		
Nonrandomized	Reference	
Randomized	1.44 (0.87–2.38)	.16
Oversight by a data safety monitoring committee		
No	Reference	
Yes	1.23 (0.87–1.74)	.25
Location		
Low- and middle-income countries only	Reference	
High-income countries	2.04 (1.34–3.13)	<.001
Number of facilities		
1	Reference	
>2	1.74 (1.18–2.56)	.005

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

(continued)

SUPPLEMENTAL TABLE 6

Univariable analyses of association between trial features and results reporting within 3 years of completion *(continued)*

Trail feature	Odds ratio (95% confidence interval)	*P* value
Therapeutic focus[e]		
All other therapeutic foci	Reference	
Cesarean delivery	1.55 (1.01–2.37)	.043
Nutrition	0.56 (0.31–0.99)	.046
Anesthesia	1.52 (0.95–2.42)	.08
Infection	1.12 (0.67–1.87)	.67
Fetal	1.16 (0.63–2.13)	.63
Mental health	1.01 (0.53–1.95)	.97
Early delivery	0.87 (0.39–1.94)	.74
Diabetes mellitus	0.75 (0.35–1.58)	.45

[a] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency United States government trials include remaining trials with a United States government sponsor or collaborating agency; [b] Other primary purposes include diagnostic, screening, supportive care, health services research, and other; [c] On ClinicalTrials.gov, "Not Applicable" is used to describe trials without Food and Drug Administration–defined phases, including trials of devices or behavioral interventions; [d] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment); [e] Trials could have >1 therapeutic focus. For analysis, each therapeutic focus was treated as a binary variable.

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021.

SUPPLEMENTAL TABLE 7
Association between trial features and results reporting within 3 years of completion

Trial feature	Odds ratio (95% confidence interval)	*P* value
All trials		
Nonobstetrical	Reference	
Obstetrical	0.89 (0.72–1.10)	.19
Obstetrical trials only		
Funding[a]		
Industry	Reference	
Academic	0.39 (0.22–0.68)	.0009
United States government	1.06 (0.53–2.09)	.87
Primary purpose		
Treatment	Reference	
Basic science	1.49 (0.62–3.56)	.37
Prevention	0.98 (0.65–1.47)	.92
Other[b]	0.85 (0.51–1.43)	.54
Phase		
Phase 2/3–3	Reference	
Not Applicable[c]	0.82 (0.47–1.43)	.49
Phase 1	0.89 (0.34–2.39)	.82
Phase 1/2–2	1.91 (0.99–3.70)	.05
Phase 4	0.92 (0.47–1.79)	80
Enrollment[d]		
100–499	Reference	
0–9	0.44 (0.05–3.56)	.44
10–49	1.08 (0.66–1.76)	.77
50–99	0.86 (0.55–1.35)	.53
500–999	0.62 (0.28–1.37)	.24
>999	0.61 (0.31–1.21)	.16
Blinding		
None	Reference	
Double	0.82 (0.52–1.31)	.41
Single	0.90 (0.58–1.39)	.63
Randomization		
Nonrandomized	Reference	
Randomized	1.36 (0.81–2.28)	.25
Oversight by a data safety monitoring committee		
No	Reference	
Yes	1.41 (0.98–2.04)	.07
Location		
Low- and middle-income countries only	Reference	
High-income countries	2.13 (1.35–3.36)	.001

Steinberg et al. The obstetrical clinical trial landscape. AJOG MFM 2021. *(continued)*

SUPPLEMENTAL TABLE 7
Association between trial features and results reporting within 3 years of completion *(continued)*

Trial feature	Odds ratio (95% confidence interval)	*P* value
Number of facilities		
1	Reference	
≥2	1.22 (0.80–1.87)	.35
Therapeutic focus[e]		
All other therapeutic foci	Reference	
Cesarean delivery	2.07 (1.29–3.34)	.003
Nutrition	0.75 (0.44–1.29)	.30
Anesthesia	1.07 (0.62–1.87)	.80
Infection	1.25 (0.75–2.09)	.39
Fetal	0.75 (0.37–1.53)	.43
Mental health	0.51 (0.23–1.12)	.09
Early delivery	0.51 (0.23–1.12)	.88
Diabetes mellitus	0.83 (0.39–1.77)	.63

[a] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency United States government trials include remaining trials with a United States government sponsor or collaborating agency; [b] Other primary purposes include diagnostic, screening, supportive care, health services research, and other; [c] On ClinicalTrials.gov, "Not Applicable" is used to describe trials without Food and Drug Administration–defined phases, including trials of devices or behavioral interventions; [d] Enrollment included both actual enrollment (for completed trials) and anticipated enrollment (for ongoing trials with continued enrollment); [e] Trials could have >1 therapeutic focus. For analysis, each therapeutic focus was treated as a binary variable.

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SUPPLEMENTAL TABLE 8
Results reporting among trials completed by March 9, 2017[a]

	Completed trials	Results reported by March 9, 2020
Total	1411	216 (15.3)
funding[b]		
Industry	102	29 (28.4)
Academic	1171	149 (12.7)
United States government	138	38 (27.5)

Values are number (percentage) unless indicated otherwise.

[a] Only trials completed by March 8, 2017, were included in the analysis of results reporting to align with federal mandates for delayed submission of results information within 3 years of trial completion; [b] Funding categories were determined with data on the sponsor and collaborators. Industry funding includes trials with an industry sponsor or collaborating agency. United States government trials include remaining trials with a United States government sponsor or collaborating agency. Academic trials include all other trials.

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