Appendix 1. Search Strategy

Literature Databases: Ovid MEDLINE, Embase, CINAHL, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews were searched. Detailed search strategies are listed below.

Publication Date Range: Searches were conducted across all Key Questions, with study dates reaching back to the inception of each database up to October 2019, with an updated search done through July 2020. Searches were deduplicated and screened for inclusion.

Supplemental Evidence and Data for Systematic review (SEADS): Manufacturers and other stakeholders of included drugs and devices were informed about submitting information relevant to this review using a Federal Register notification. A portal about the opportunity to submit information was made available on the Effective Health Care (EHC) website. We received two submissions, one from the review sponsor, ACOG, and one from Ferring Pharmaceuticals. While both were supportive of this research effort, neither included citations for evidence to consider. Additionally, after the public review period closed, we received another submission from Medicem, Inc. which included citations for Dilapan-S; all citations were reviewed and none met the inclusion criteria for this report.

Hand Searching: Reference lists of included articles were reviewed for includable studies.

Medline Search

Databases: Ovid MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions 1946 to October 9, 2019; updated search to July 27, 2020

Randomized Controlled trials and Systematic Reviews

1 Pregnant Women/
2 pregnancy/ or labor, obstetric/ or pregnancy outcome/
3 pregnan*.ti,ab,kf.
4 Labor, Induced/
5 Cervical Ripening/
6 ((cervi* or labor or labour) adj3 (induction or induce* or ripening or priming)).ti,ab,kf.
7 ((foley or cook or balloon) adj3 catheter).ti,ab,kf.
8 ((foley or cook) adj3 balloon).ti,ab,kf.
9 7 or 8
10 Misoprostol/
11 Dinoprostone/
12 (misoprostol or dinoprostone or "prostaglandin E1" or "prostaglandin E2" or PGE1 or PGE2 or "hygroscopic dilator*" or dilapan or "laminaria tent*").ti,ab,kf.

13 Outpatients/
14 (outpatient* or "out of hospital").ti,ab,kf.
15 or/1-3
16 or/4-6,9-12
17 or/13-14
18 16 and 17
19 15 and 16
20 randomized controlled trial.pt.
21 (random* or control* or placebo or sham or trial).ti,ab,kw.
22 (systematic or "meta analysis" or metaanalysis or review or cochrane).ti,ab,kf.
23 20 or 21 or 22
24 19 and 23
25 limit 24 to english language
26 (animal* or mouse or mice or rat* or dog* or canine or cow* or bovine or horse* or mare* or pig* or porcine or rabbit* or llama* or sheep or ewe*).ti.
27 25 not 26

Cohort and case-control studies

1 Pregnant Women/
2 pregnancy/ or labor, obstetric/ or pregnancy outcome/
3 pregnan*.ti,ab,kf.
4 Labor, Induced/
5 Cervical Ripening/
6 ((cervi* or labor or labour) adj3 (induction or induce* or ripening or priming)).ti,ab,kf.
7 ((foley or cook or balloon) adj3 catheter).ti,ab,kf.
8 ((foley or cook) adj3 balloon).ti,ab,kf.
9 7 or 8
10 Misoprostol/
11 Dinoprostone/
12 (misoprostol or dinoprostone or "prostaglandin E1" or "prostaglandin E2" or PGE1 or PGE2 or "hygroscopic dilator*" or dilapan or "laminaria tent*").ti,ab,kf.
13 Outpatients/
14 (outpatient* or "out of hospital").ti,ab,kf.
15 or/1-3
16 or/4-6,9-12
17 or/13-14
18 16 and 17
19 15 and 16
20 (animal* or mouse or mice or rat* or dog* or canine or cow* or bovine or horse* or mare* or pig* or porcine or rabbit* or llama* or sheep or ewe*).ti.
21 19 not 20

22 exp cohort studies/
23 (cohort* or prospective or observational).tw.
24 controlled clinical trial.pt.
25 epidemiologic methods/
26 limit 25 to yr=1966-1989
27 exp case-control studies/
28 (case$ and control$).tw.
29 or/22-24,26-28
30 21 and 29
31 30 not (abortion or terminate or termination).ti.
32 limit 31 to english language

Cochrane Central Register of Controlled Trials Search

Database: EBM Reviews - Cochrane Central Register of Controlled Trials to September 2019; updated search to July 27, 2020

1 Pregnant Women/
2 pregnancy/ or labor, obstetric/ or pregnancy outcome/
3 pregnan*.ti,ab.
4 Labor, Induced/
5 Cervical Ripening/
6 ((cervi* or labor or labour) adj3 (induction or induce* or ripening or priming)).ti,ab.
7 ((foley or cook or balloon) adj3 catheter).ti,ab.
8 ((foley or cook) adj3 balloon).ti,ab.
9 7 or 8
10 Misoprostol/
11 Dinoprostone/
12 (misoprostol or dinoprostone or "prostaglandin E1" or "prostaglandin E2" or PGE1 or PGE2 or "hygroscopic dilator*" or dilapan or "laminaria tent*").ti,ab.
13 Outpatients/
14 (outpatient* or "out of hospital").ti,ab.
15 or/1-3
16 or/4-6,9-12
17 or/13-14
18 15 and 16 and 17
19 limit 18 to (journal article or meta analysis or randomized controlled trial)
20 limit 19 to english language

Cochrane Database of Systematic Reviews Search

Database: EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 9, 2019; updated search to July 27, 2020

1 ((cervi* or labor or labour) adj3 (induction or induce* or ripening or priming)).ti.
2 ((foley or cook or balloon) adj3 catheter).ti,ab.
3 (misoprostol or dinoprostone or "prostaglandin E1" or "prostaglandin E2" or PGE1 or PGE2 or "hygroscopic dilator*" or dilapan or "laminaria tent*").ti.
4 ((foley or cook or balloon) and (pregnan* or labor or labour or cervi*)).ti,ab.
5 or/1-4
6 limit 5 to full systematic reviews

CINAHL Search

Database: CINAHL Plus with Full Text to October 9, 2019; updated search to July 27, 2020

S1 (MH "Labor, Induced")
S2 (MH "Cervix Dilatation and Effacement")
S3 (MH "Misoprostol")
S4 (MH "Dinoprostone")
S5 cervi OR cervical
S6 ripening
S7 S5 AND S6
S8 misoprostol OR dinoprostol OR prostaglandin E1 OR prostaglandin E2 OR PGE1 OR PGE2 OR hygroscopic dilator or dilapan or laminaria tent
S9 foley OR cook OR balloon
S10 catheter*
S11 S9 AND S10
S12 S1 OR S2 OR S3 OR S4
S13 S7 OR S8 OR S11
S14 S12 OR S13
S15 pregnan* OR labor OR labour
S16 S11 AND S15
S17 S7 OR S8 OR S16
S18 S12 OR S17
S19 S12 OR S17
Limiters - English Language; Exclude MEDLINE records; Human

Embase Search

Database: Elsevier Embase to October 9, 2019; updated search to July 2020

('labor induction'/exp AND ('misoprostol'/exp OR 'prostaglandin e2'/exp OR 'foley balloon catheter'/exp) OR 'uterine cervix ripening'/exp OR 'cervical ripening':ab,ti) AND [english]/lim AND ('article'/it OR 'article in press'/it) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)

Appendix 2. Population, Interventions, Comparators, Outcomes, Timing, and Settings/Study Design (PICOTS) Table

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs. Outpatient	Inclusion Key Question 3: Outpatient Comparison of Methods	Exclusion
Population	Pregnant women ≥37 weeks undergoing cervical ripening in the outpatient setting Important maternal subgroups: parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational) Important fetal subgroups: fetal growth restriction, gestational age (<39 weeks, 39 to 41 weeks, >41 weeks)	Pregnant women ≥37 weeks undergoing cervical ripening in the outpatient setting Important maternal subgroups: parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational) Important fetal subgroups: fetal growth restriction, gestational age (<39 weeks, 39 to 41 weeks, >41 weeks)	Pregnant women ≥37 weeks undergoing cervical ripening in the outpatient setting Important maternal subgroups: parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational) Important fetal subgroups: fetal growth restriction, gestational age (<39 weeks, 39 to 41 weeks, >41 weeks)	Women with contraindications to cervical ripening in the outpatient setting: a multiple pregnancy, prior uterine rupture and breech presentation of the fetus.

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs. Outpatient	Inclusion Key Question 3: Outpatient Comparison of Methods	Exclusion
Intervention	Pharmacologic agents (prostaglandins) given in outpatient setting	Mechanical methods (balloon catheters, laminaria tents) used in outpatient setting	Mechanical methods (balloon catheters, laminaria tents) or pharmacologic agents (prostaglandins)	Catheters not available in the U.S. Pharmacy-compounded prostaglandin products Other cervical ripening methods: Castor oil, nipple stimulation, membrane stripping, sexual intercourse, acupuncture/pressure, transcutaneous nerve stimulation, herbal compounds
Comparator	Mechanical (i.e., balloon catheters, laminaria tents) and/or pharmacologic (i.e., prostaglandins) methods in the inpatient setting	Mechanical (i.e., balloon catheters, laminaria tents) and/or pharmacologic (i.e., prostaglandins) methods in the inpatient setting	Any comparator including alternative mechanical device or protocol, alternative pharmacologic agent or dose, combination mechanical and pharmacologic, placebo, and other cervical ripening methods excluded as intervention (e.g., Castor oil, acupuncture)	Catheters not available in the U.S. Pharmacy-compounded prostaglandin products

Outcomes Effectiveness (birth-related)	**Total time admission to vaginal birth; total L&D length of stay**[‡] **Cesarean delivery rate overall**[‡] Vaginal birth within 24 hours Failed induction rate, defined as: Cesarean delivery in patient at <6cm dilation excluding fetal distress (labor dystocia, failure to progress, etc.) Cesarean delivery in patient at <6 cm dilation for fetal distress Cervical assessment at time of admission (e.g., latent vs. active phase, Bishop score, cervical dilation) Time from ROM to delivery	**Total time admission to vaginal birth; total L&D length of stay**[‡] **Cesarean delivery rate overall**[‡] Vaginal birth within 24 hours Failed induction rate, defined as: Cesarean delivery in patient at <6cm dilation excluding fetal distress (labor dystocia, failure to progress, etc.) Cesarean delivery in patient at <6 cm dilation for fetal distress Cervical assessment at time of admission (e.g., latent vs. active phase, Bishop score, cervical dilation) Time from ROM to delivery	**Total time admission to vaginal birth; total L&D length of stay**[‡] **Cesarean delivery rate overall**[‡] Vaginal birth within 24 hours Failed induction rate, defined as: Cesarean delivery in patient at <6cm dilation excluding fetal distress (labor dystocia, failure to progress, etc.) Cesarean delivery in patient at <6 cm dilation for fetal distress Cervical assessment at time of admission (e.g., latent vs. active phase, Bishop score, cervical dilation) Time from ROM to delivery Breastfeeding[†] Maternal mood[†] Mother-baby attachment[†]	Outcomes not listed in inclusion criteria
Outcomes Fetal Harms	**Perinatal Mortality**[‡] **Hypoxic-ischemic encephalopathy**[‡]	**Perinatal Mortality**[‡] **Hypoxic-ischemic encephalopathy**[‡]	**Perinatal Mortality**[‡] **Hypoxic-ischemic encephalopathy**[‡]	Outcomes not listed in inclusion criteria

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs. Outpatient	Inclusion Key Question 3: Outpatient Comparison of Methods	Exclusion
	Seizure[‡] **Infection** (confirmed sepsis or pneumonia)[‡] **Meconium aspiration syndrome**[‡] **Birth trauma** (e.g., bone fracture, neurologic injury, or retinal hemorrhage)[‡] **Intracranial or subgaleal hemorrhage**[‡] Need for respiratory support within 72 hours after birth Apgar score ≤3 at 5 minutes[*] Hypotension requiring vasopressor support Umbilical cord gas < pH 7.0 or 7.10	**Seizure**[‡] **Infection** (confirmed sepsis or pneumonia)[‡] **Meconium aspiration syndrome**[‡] **Birth trauma** (e.g., bone fracture, neurologic injury, or retinal hemorrhage)[‡] **Intracranial or subgaleal hemorrhage**[‡] Need for respiratory support within 72 hours after birth Apgar score ≤3 at 5 minutes[*] Hypotension requiring vasopressor support Umbilical cord gas < pH 7.0 or 7.10	**Seizure**[‡] **Infection** (confirmed sepsis or pneumonia)[‡] **Meconium aspiration syndrome**[‡] **Birth trauma** (e.g., bone fracture, neurologic injury, or retinal hemorrhage)[‡] **Intracranial or subgaleal hemorrhage**[‡] Need for respiratory support within 72 hours after birth Apgar score ≤3 at 5 minutes[*] Hypotension requiring vasopressor support Umbilical cord gas < pH 7.0 or 7.10	

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs. Outpatient	Inclusion Key Question 3: Outpatient Comparison of Methods	Exclusion
Outcomes Maternal Harms	**Hemorrhage requiring transfusion**‡ **Postpartum hemorrhage by mode** (vaginal, cesarean delivery)‡ **Uterine infection** (i.e., choriamnionitis, administration of antibiotics in labor other than GBS prophylaxis)‡ Placental abruption Uterine rupture Umbilical cord prolapse Duration of time between hospital admission to birth that is insufficient to enable complete GBS prophylaxis antibiotics administration per CDC guidelines	**Hemorrhage requiring transfusion**‡ **Postpartum hemorrhage by mode** (vaginal, cesarean delivery)‡ **Uterine infection** (i.e., choriamnionitis, administration of antibiotics in labor other than GBS prophylaxis)‡ Placental abruption Uterine rupture Umbilical cord prolapse Duration of time between hospital admission to birth that is insufficient to enable complete GBS prophylaxis antibiotics administration per CDC guidelines	**Hemorrhage requiring transfusion**‡ **Postpartum hemorrhage by mode** (vaginal, cesarean delivery)‡ **Uterine infection** (i.e., choriamnionitis, administration of antibiotics in labor other than GBS prophylaxis)‡ Placental abruption Uterine rupture Umbilical cord prolapse Duration of time between hospital admission to birth that is insufficient to enable complete GBS prophylaxis antibiotics administration per CDC guidelines	Outcomes not listed in inclusion criteria

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs. Outpatient	Inclusion Key Question 3: Outpatient Comparison of Methods	Exclusion
Timing	Maternal outcomes From cervical ripening initiation to within 1 week following delivery Infant outcomes Immediately following delivery	Maternal outcomes From cervical ripening initiation to within 1-week following delivery Infant outcomes Immediately following delivery.	Maternal and additional outcomes (i.e., breastfeeding, maternal mood, mother-baby attachment) From cervical ripening initiation to 1-year postpartum Infant outcomes Immediately following delivery	KQ 1,2,4: Outcomes occurring after 1-week post delivery KQ3: Outcomes for breastfeeding, mother-infant attachment, and maternal mood occurring after 1 year post-delivery.
Setting	Inpatient versus outpatient settings	Inpatient versus outpatient settings	Outpatient setting	
Study design	RCTs; recent high-quality SRs; if RCT evidence for benefits is insufficient, include large, high quality cohort studies comparing inpatient and outpatient setting. Include high quality cohort and case-control studies for harms.	RCTs; recent high-quality SRs; if RCT evidence for benefits is insufficient, include large, high quality cohort studies comparing inpatient and outpatient setting. Include high quality cohort and case-control studies for harms.	RCTs; recent high-quality SRs; if RCT evidence for benefits is insufficient, include large, high quality cohort studies comparing inpatient and outpatient setting. Include high quality cohort and case-control studies for harms.	Case series, pre-post studies, case reports

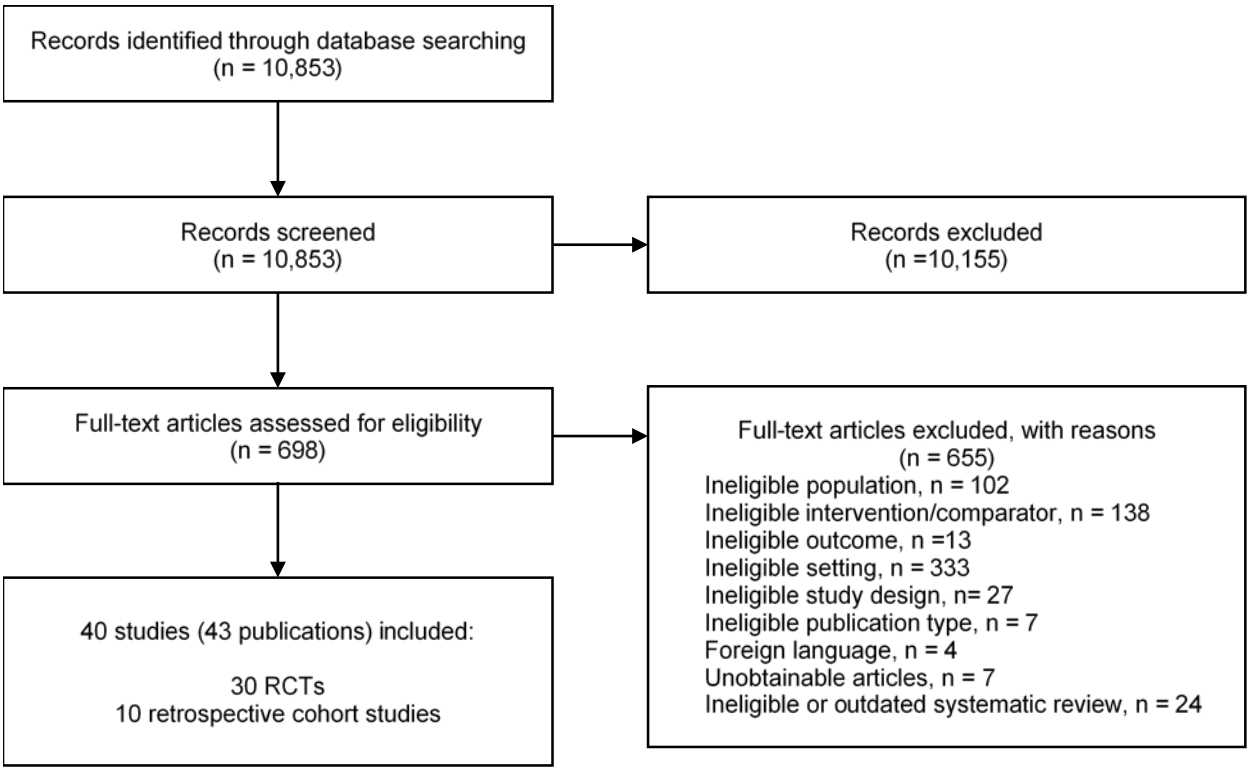
PICOTS = population, interventions, comparators, outcomes, timing, and settings/study design; GBS = Group B Streptococcus; L&D = labor and delivery; ROM = rupture of membrane; CDC = Centers for Disease Control and Prevention; KQ = Key Question; RCT = randomized controlled trial; SR = systematic review

* Allowed higher thresholds from older studies if inadequate evidence with this threshold

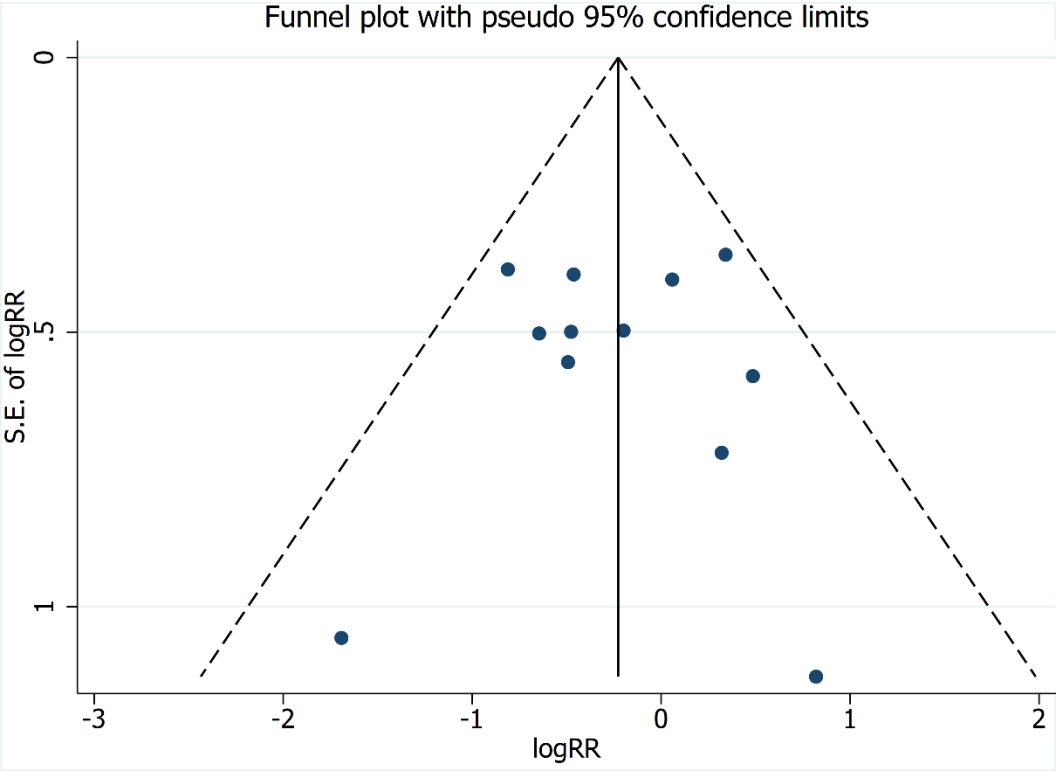
† Specific to Key Question 3

‡ **(Bolded) items indicate Primary Outcomes**

Appendix 3. Literature flow diagram. RCT, randomized controlled trial.



Appendix 4. Publication bias plot (funnel plot) of cesarean delivery prostaglandins compared with placebo for cervical ripening in the outpatient setting. SE, standard error; RR, relative risk.



McDonagh M, Skelly AC, Tilden E, Brodt ED, Dana T, Hart E, et al. Outpatient cervical ripening: a systematic review and meta-analysis. Obstet Gynecol 2021;137.
The authors provided this information as a supplement to their article.