Guidelines on Deferred Cord Clamping and Cord Milking: A Systematic Review

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abstract

CONTEXT: Deferred cord clamping (DCC) saves lives. It reduces extremely preterm infants’ mortality by 30%, yet a minority of eligible infants receive it. This may in part be due to lack of awareness or confidence in evidence, or conflicting or vague guidelines.

OBJECTIVE: To systematically review clinical practice guidelines and other statements on DCC and cord milking.

DATA SOURCES: Ten academic and guideline databases were searched.

STUDY SELECTION: Clinical practice guidelines and other statements (position statements and consensus statements) providing at least 1 recommendation on DCC or umbilical cord milking among preterm or term infants were included.

DATA EXTRACTION: Data from included statements were extracted by 2 independent reviewers, and discrepancies were resolved through consensus. Guideline quality was appraised with modified Appraisal of Guidelines for Research and Evaluation II and Appraisal of Guidelines for Research and Evaluation Recommendation Excellence tools.

RESULTS: Forty-four statements from 35 organizations were included. All endorsed DCC for uncompromised preterm infants, and 11 cautiously stated that cord milking may be considered when DCC is infeasible. Only half (49%) of the recommendations on the optimal duration of DCC were supported by high-quality evidence. Only 8% of statements cited a mortality benefit of DCC for preterm infants.

LIMITATIONS: Because systematic reviews of guidelines are relatively novel, there are few tools to inform study execution; however, we used the Appraisal of Guidelines for Research and Evaluation II and the Appraisal of Guidelines for Research and Evaluation Recommendation Excellence to assess quality and were methodologically informed by previous systematic reviews of guidelines.

CONCLUSIONS: Statements worldwide clearly encouraged DCC. Their implementability would benefit from noting the preterm mortality benefit of DCC and more granularity.

Cutting the umbilical cord is inevitable; but should it be rushed? Deferred cord clamping (DCC) facilitates the newborn infant’s transition to extraterine life by allowing fetoplacental circulation to continue as the lungs expand after birth.1 Umbilical cord milking (UCM) is when blood in the cut or uncut cord is squeezed toward the infant.2

DCC reduces neonatal morbidity and mortality, especially among preterm infants. In a systematic review of 18 randomized controlled trials (RCTs), DCC (defined as ≥30 seconds) reduced the risk of mortality by 32% in preterm infants.3 RCTs revealed that DCC reduced the risks of intraventricular hemorrhage (IVH), necrotizing enterocolitis, and sepsis among preterm infants; reduced the need for blood transfusions and respiratory support; improved iron stores at 3 to 6 months; and improved neurodevelopmental outcomes at 2 years.3-6

In a systematic review of 7 RCTs, UCM reduced the risks of IVH and oxygen requirement and improved hemoglobin levels among preterm infants.7 However, a recent large RCT raised concerns about the risks of IVH with UCM.8-10

DCC is a simple and inexpensive practice,9,10 yet many health providers are reluctant to defer clamping.11,12 In California, at least 42% of preterm infants (gestational age <32 weeks or birth weight <1500 g) admitted to neonatal intensive care in 2016 did not receive DCC.13 In Canada, 40% of preterm infants and 53% of extremely preterm infants admitted to a NICU in 2018 did not receive DCC.14 This may be, in part, because of the persistence of custom, lack of awareness or confidence in evidence, and conflicting or vague guidelines.15 To address the latter three issues, we systematically described the clinical guidance on placental transfusion to identify gaps in guidance, concordance with evidence available at the time (including benefits for preterm mortality),3 and recommendation quality.

METHODS
We conducted this systematic review (PROSPERO identifier CRD42019143332) according to available methodological guidance on conducting a systematic review of guidelines.16,17

Data Sources
We searched the following 10 academic and guideline databases from January 1, 2010, to July 17, 2019 (Supplemental Table 2): Ovid Medline, Ovid Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Central Register of Controlled Trials, Web of Science, Clinical Practice Guideline (CPG) Infobase, Guidelines International Network, National Institute for Health and Care Excellence (NICE) Evidence, Royal College of Obstetricians and Gynaecologists Guidance, and Trip Medical Database. We hand searched the Web sites of members of the International Federation of Gynaecology and Obstetrics that had Web sites with recommendation statements (Supplemental Table 3).

Inclusion Criteria
With no language restrictions, we included the most recent versions of CPGs and other recommendation statements published after 2010 that provide at least 1 recommendation on DCC or UCM among preterm or term infants. On the basis of the definition provided by the Institute of Medicine, we defined CPGs as statements developed by a dedicated multidisciplinary panel, after a thorough review of the evidence, to optimize patient and practitioner decisions.10 We also reported on other statements that could not be described as CPGs (position statements and consensus statements) in order to comprehensively summarize all recommendations that inform health providers’ cord management practices.

Data Extraction
Two reviewers (S.K.L. and K.N.) independently screened the titles and abstracts and full texts. Data from included full texts regarding guideline authorship, guideline development methodology, DCC and UCM recommendations, and sources of evidence supporting the recommendations were abstracted by using a piloted data extraction form. Discrepancies were discussed between reviewers to reach consensus, and a third reviewer (S.D.M) was consulted, as necessary.

Quality Assessment
Two reviewers independently appraised the quality of included statements using the modified Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument (Supplemental Table 4).19 AGREE II was modified to only include 3 of the 6 domains (scope and purpose, clarity of presentation, and editorial independence). The remaining 3 domains (stakeholder involvement, rigor of development, and applicability) were removed for 3 key reasons. First, only 3 domains were scored so that the AGREE II appraisal highlights the quality of cord management recommendations specifically (rather than the quality of recommendations on other topics as well), thus more accurately reflecting our research topic. Second, we wanted to prevent bias toward assessing the few guidelines dedicated to cord management as higher quality than the majority of guidelines, which had a broader or different focus (eg, preterm labor) and, thus, less comprehensive recommendations on cord management. Finally, because the reviewers were not experienced in all topics addressed by the guidelines (eg, neonatal resuscitation), we wanted to avoid arbitrary scoring
of areas in which we lacked knowledge.

The clinical credibility and implementability of the relevant recommendations on cord management were appraised by using Appraisal of Guidelines for Research and Evaluation Recommendation Excellence (AGREE-REX) (Supplemental Table 4), which comprises 3 domains (clinical applicability, values and preferences, and implementability). We also applied AGREE II and AGREE-REX to position papers and consensus statements. Although it is important to note that these statements will inherently receive lower-quality assessments because they do not follow the rigorous CPG development methodology that Appraisal of Guidelines for Research and Evaluation (AGREE) is designed to assess, we wanted to appraise all statements using a consistent framework.

AGREE advises users to determine their own thresholds to interpret scores according to the context of their study. Hence, in line with a number of other systematic reviews of CPGs, we considered domain scores ≥50% to be consistent with higher quality and domain scores <50% to be consistent with lower quality. Because different domains were not equally relevant in our study, we did not pool together domain scores, and instead we reported individual domain scores.

**Data Analysis**

We calculated the proportion of statements that recommended DCC and UCM for preterm or term infants. We reported on the details of the recommendations and their concordance with the highest level of evidence available at the time of publication regarding the mortality benefit of DCC among preterm infants because we hypothesized that physicians would be more likely to employ DCC if it is supported by this type of evidence.

**RESULTS**

The searches retrieved 4765 records (Fig 1). After excluding 1540 duplicates, we screened 3225 titles and abstracts and selected 311 records for full-text screening. Before resolving discrepancies, the reviewers had 97% agreement for inclusion and exclusion of full texts. We included 44 statements, of which 24 met the criteria for a CPG because they were developed by a dedicated national or international panel after a systematic search and synthesis of the evidence to inform practitioner and patient decisions. Twenty statements were described as position papers or consensus statements or could not be confirmed to be a CPG because of a lack of detail on guideline development methodology or lack of a comprehensive evidence search (Supplemental Table 5). The included statements represented the views of 35 national and international professional societies, commonly in the fields of obstetrics, midwifery, neonatology, pediatrics, and resuscitation. Statements addressed a global audience but predominantly high-income countries: 33 of 44 addressed 17 different high-income

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**FIGURE 1**

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of a systematic review of CPGs and other recommendation statements on DCC and UCM. The flow of studies is summarized through the following stages in the systematic review: database searching, title and abstract screening, and full-text screening.
countries, 4 specifically addressed Europe, 5 addressed 5 different middle-income countries, and 3 had a global focus (Fig 2). The available clinical guidelines on DCC and UCM are summarized in Figure 3 and described in detail below.

### Quality of Statements

Detailed and summarized AGREE II and AGREE-REX scores are listed in Supplemental Table 4. On the modified AGREE II instrument to assess methodologic rigor, 18 of the 44 (41%) statements had high quality in all 3 domains (scope and purpose, clarity of presentation, and editorial independence). On the AGREE-REX instrument to assess the quality of recommendations, 11 statements (25%) were high quality in all 3 domains (clinical applicability, values and preferences, and implementability). Eight statements (18%) had high quality in all domains of AGREE II and AGREE-REX, with statements by NICE32 and the World Health Organization (WHO)41 having the highest scores overall.

On AGREE-REX, clinical applicability is used to assess the quality of the evidence review and applicability to clinicians and patients: 31 statements scored high quality in this domain. Values and preferences was the weakest domain overall (only 11 statements scoring high quality); it is used to assess efforts taken to make recommendations and outcomes important to clinicians, patients, and policy- and decision-makers.
Recommendations on DCC

Summary of DCC Recommendations

Forty-four statements contained a total of 70 recommendations on DCC for subpopulations (Supplemental Fig 5); 24 recommendations were specific to preterm infants, with 3 for extremely preterm infants (<28 weeks), 29,33,62 and 3 addressing extremely preterm and moderately preterm infants.23,30,55 Thirty-one applied to both preterm and term infants, and 15 applied only to term infants (>37 weeks). Two recommendations were specific for multiple gestations.23,24

Three recommendations did not explicitly endorse DCC in certain instances. First, a committee opinion by the American College of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice stated that there is insufficient evidence to recommend for or against DCC in multiple gestations.24 Second, a CPG by the Society of Obstetricians and Gynaecologists of Canada stated that in term infants, the benefits of DCC must be balanced with the risks of neonatal jaundice requiring phototherapy.43 Finally, a CPG by the Italian Task Force for the Management of Umbilical Cord Clamping recommended immediate clamping in directed cord blood collection for at-risk families.23

Regarding mode of delivery, 3 recommendations on preterm infants,23,57 3 on term infants,23,25,57 and 1 on both preterm or term infants provided recommendations specific to DCC after cesarean delivery (CD).57

Optimal Timing To Defer Clamping

Fifty-one of 67 (76%) recommendations endorsing DCC made a recommendation regarding the optimal duration to defer clamping (Fig 4, Supplemental Fig 5). The shortest evidence-based

<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Type of Statement (Sources of Evidence)</th>
<th>Cord Management Guidance Summary</th>
<th>AGREE D1</th>
<th>AGREE D2</th>
<th>AGREE D3</th>
<th>AGREE D4</th>
<th>AGREE D5</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Swiss Society of Neonatology (GA &gt;34 wk and BW &gt;2000 g)</td>
<td>Cannot confirm whether a CPG (Literature search + international guidelines + stakeholder opinion)</td>
<td>✕ PT (VD), T ✖ PT (CD)</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2016</td>
<td>Queensland Clinical Guidelines (Australia)</td>
<td>CPG (Literature search on multiple databases + national and international guidelines)</td>
<td>✕ PT, T ✖ PT, T</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2015</td>
<td>Dutch Resuscitation Council (adults, children, and newborns)</td>
<td>Inferred to be a CPG, cannot confirm (Literature search + stakeholder opinion)</td>
<td>✕ “Unthreatened” PT</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2015</td>
<td>European Resuscitation Council#</td>
<td>Cannot confirm whether CPG (National and international guidelines including ILCOR) + Previously evaluated evidence</td>
<td>✕ PT, T ✖ X routine practice GA &lt;28 wk</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>2015</td>
<td>ILCOR (multinational)</td>
<td>Not a CPG (Systematic review in PubMed, Embase, Cochrane Library + stakeholder opinion)</td>
<td>✕ PT ✖ X routine practice GA &lt;28 wk</td>
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<td>✗</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>2015</td>
<td>Japanese Resuscitation Council##</td>
<td>CPG (Literature search on multiple databases + ILCOR meeting discussion)</td>
<td>✕ PT ✖ X routine practice GA &lt;28 wk</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
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<td>✗</td>
</tr>
<tr>
<td>2015</td>
<td>Resuscitation Council UK###</td>
<td>CPG (Literature search + stakeholder opinion)</td>
<td>✕ PT, T ✖ X PT and/or T routine practice</td>
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<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2012</td>
<td>WHO####</td>
<td>CPG (Literature search and systematic review in multiple databases)</td>
<td>✕ PT, T</td>
<td>✗</td>
<td>✗</td>
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Preventing and Managing Postpartum Hemorrhage and AMTSL

<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Type of Statement (Sources of Evidence)</th>
<th>Cord Management Guidance Summary</th>
<th>AGREE D1</th>
<th>AGREE D2</th>
<th>AGREE D3</th>
<th>AGREE D4</th>
<th>AGREE D5</th>
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<tbody>
<tr>
<td>2019</td>
<td>Queensland Clinical Guidelines (Australia)</td>
<td>CPG (Literature search on multiple databases + national and international guidelines)</td>
<td>✕ PT, T; in AMTSL</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>2018</td>
<td>SOGC##</td>
<td>CPG (Literature search on multiple databases)</td>
<td>✕ PT (GA &lt;37 wk); T (weigh risk of jaundice with benefits of DCC)</td>
<td>✗</td>
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<td>✗</td>
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<tr>
<td>2016</td>
<td>Association of Ontario Midwives (Canada)##</td>
<td>CPG (Literature search on Medline, CINAHL, Cochrane Library)</td>
<td>✕ PT, T; in AMTSL</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>2014</td>
<td>Chinese Association of Obstetrics and Gynecology##</td>
<td>Not a CPG (International guidelines)</td>
<td>✕ PT, T</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2012b</td>
<td>WHO####</td>
<td>CPG (Literature search in Cochrane Library + stakeholder opinion)</td>
<td>✕ PT, T</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>2012</td>
<td>Federation of Obstetric and Gynaecological Societies of India####</td>
<td>Consensus statement (Clinical experience of authors)</td>
<td>✕ PT, T</td>
<td>✗</td>
<td>✗</td>
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Normal Birth (Spontaneous, Vertex, Term, Healthy Mother and Newborn) and Care of the Healthy Newborn

<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Type of Statement (Sources of Evidence)</th>
<th>Cord Management Guidance Summary</th>
<th>AGREE D1</th>
<th>AGREE D2</th>
<th>AGREE D3</th>
<th>AGREE D4</th>
<th>AGREE D5</th>
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<tbody>
<tr>
<td>2018</td>
<td>Austrian Society of Pediatrics and Adolescent Medicine#</td>
<td>Position paper (Not stated)</td>
<td>✕ T ✖ PT</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2017</td>
<td>Queensland Clinical Guidelines (Australia)</td>
<td>CPG (Literature search in multiple databases + stakeholder opinion)</td>
<td>✕ T (VD)</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>2016</td>
<td>SOGC#</td>
<td>CPG (Literature search in PubMed, Cochrane Library)</td>
<td>✕ T, T</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
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</tbody>
</table>

FIGURE 2

(Continued)
durations included 30 to 60 seconds in preterm infants, 30 to 60 seconds in term infants, and ≤30 seconds in preterm and term infants. The longest evidence-based durations included 30 to 180 seconds in preterm infants, until cord pulsation ceases in term infants, and $60$ seconds in preterm and term infants. The most commonly recommended lower limit of optimal duration was at least a minute (20 recommendations), whereas 10 recommendations suggested an upper limit of at most a minute.

Among the 51 recommendations that included an optimal timing, we reviewed the sources of evidence that the authors cited to support the suggested time (Supplemental Fig 5). For 11 timings (22%), a source of evidence was not cited. In 25 (50%), primary studies or systematic reviews were cited. In 6 (12%), the authors cited other guidelines rather than primary research. For the remaining 9 (18%) recommended timings, the authors did cite evidence to support the recommendation; however, there was a mismatch between either the upper or lower limit of the durations recommended in the evidence sources and the durations recommended in the statements. Hence, we could not confidently determine if and how these recommendations were informed by the cited evidence, expert opinion, and authors’ consensus decisions (Supplemental Table 6).

**Contraindications to DCC**

Common maternal and infant contraindications to DCC included significant maternal bleeding and unstable maternal conditions (6 statements), the need for immediate neonatal resuscitation (29 statements), an infant heart rate <60 beats per minute (2 statements), and suspected fetal asphyxia (1 statement). Common uteroplacental contraindications included concerns about the integrity of the cord and placental circulation and placental abruption or previa (7 statements).

**Recommendations on UCM**

The 23 recommendations on UCM in 20 statements were more cautious and less detailed than those on DCC (Supplemental Table 7). Fifteen recommendations suggested that UCM may be considered when DCC is infeasible and when there is significant maternal bleeding, when there is a need for immediate neonatal support, or in emergency situations. Only 4 recommendations provided suggestions on the numbers of times to milk the cord, ranging from 2 to 5 times. Thirteen statements discouraged the routine use of UCM because of insufficient evidence of its benefits and harms.

**Concordance With Evidence on the Mortality Benefit of Umbilical Cord Management**

Given our hypothesis that clinicians would be more likely to change
practice on the basis of evidence revealing benefit in compelling outcomes, such as reductions in infant death, we examined the number of statements that used mortality data to justify DCC. Among the 39 statements that provided recommendations relevant to preterm infants (recommendations for preterm or both preterm and term infants), only 3 (8% of statements) reported a mortality benefit of DCC for preterm infants. Guidelines by the Italian Task Force for the Management of Umbilical Cord Clamping and the European Society for Paediatric Research both reported the findings of the systematic review by Fogarty et al, which found that DCC (mainly ≥60 seconds) significantly reduced hospital mortality in preterm infants compared with immediate cord clamping. Additionally, the 2016 guideline by the Confalonieri Ragonese Foundation cited the results of a systematic review by Backes et al, which found that DCC and UCM reduced mortality among preterm infants <32 weeks’ gestation (relative risk 0.42; 95% confidence interval 0.19–0.95).

In concordance with meta-analytic evidence, a mortality benefit for preterm infants was reported in none of the statements that provided recommendations on UCM and the AGREE-REX to appraise the methodologic quality and applicability of all recommendations.

Our study also has limitations. First, given that using guidelines as the study type is relatively new in the world of systematic reviews (although increasing), there is a lack of tools to inform study design and execution. To mediate this limitation, we closely followed methodologic guidance for systematic reviews of CPGs by Johnston et al and referred to published systematic reviews of CPGs. Second, we could not ascertain the level of authority possessed by each authoring organization, which would allow us to comment on the degree to which particular recommendations influence practitioners. Third, for feasibility, we used Google Translate to interpret guidelines not written in English, when local translation was not available, for the following languages: Estonian, French, German, Italian, Japanese, Romanian, and Spanish. Finally, because our search strategy was designed to capture guidelines that mention terms describing placental transfusion, we are unable to calculate the proportion of all perinatal guidelines that comment on cord management.

**DISCUSSION**

In this systematic review, we included 24 CPGs and 20 other statements, which together contained 70 recommendations on DCC and 23 recommendations on UCM for preterm and term infants. There was significant variation between statements on the specific details of performing DCC and UCM, despite all endorsing placental transfusion. Statements frequently failed to cite the most compelling evidence of reductions in mortality in preterm infants.

**Strengths and Limitations**

Motivated by the clinical goal of improving DCC rates by improving guideline quality, we comprehensively searched in multiple academic and gray literature sources without language or country restrictions. We included CPGs, consensus statements, and position papers; hence, we synthesized all retrieved recommendations that may shape health providers’ practices. In addition, we reviewed the concordance of recommendations with cited evidence regarding the duration of DCC and the availability of high-quality evidence on the mortality benefits of placental transfusion for preterm infants. Finally, we used a modified AGREE II

**FIGURE 3** Summary of recommendations on DCC and cord milking in included statements. The proportions of recommendations on DCC (including the recommended optimal durations to defer clamping) and UCM are summarized.
suggest deferring ≥30 seconds or ≥60 seconds but do not suggest an upper limit at which time to clamp the cord. One reason for this may be that because most preterm infants require early support, an optimal time to clamp the cord has not yet been established. We identified a few statements recommending clamping the cord at times that are not yet verified by robust evidence (eg, 5 minutes, after delivery of the placenta). To maximize the benefits of DCC and prevent adverse effects, recommended durations should reflect high-quality evidence.

Nearly two-thirds of the statements exclude nonvigorous infants who require immediate neonatal resuscitation from receiving DCC in order to move the infant away from the mother to perform resuscitation. Unfortunately, this means that the sickest infants, who might benefit from DCC the most, are excluded from this intervention. Innovative technological solutions that may address this issue are being studied: prototypes of mobile trolleys that allow neonatal resuscitation to be performed with an intact cord have revealed safety, feasibility, and acceptability among health providers (eg, Bedside Assessment, Stabilization and Initial Cardiorespiratory Support, LifeStart).73,74 If proven to be beneficial, bringing resuscitation to the mother’s bedside will require changes to hospital policy and ergonomics and collaboration between care providers, including pediatricians, obstetricians, and midwives.75

Beyond DCC, UCM is a potential simple alternative that can allow placental transfusion to be quickly performed in infants who need immediate resuscitation.69,75 Statements recommended UCM less frequently compared with DCC. Because milking disrupts the normal fetoplacental circulation to increase blood flow to the infant more rapidly than DCC, there are concerns that UCM may have adverse effects.76 Guidelines echoed the need for more research on UCM, some of which has recently emerged. A trial by Katheria et al18 was prematurely terminated because of concerns about severe IVH.

### Table: Recommendations on DCC by Included CPGs

<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Population</th>
<th>Contraindications</th>
<th>Recommendations on DCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>Enhanced Recovery After Surgery Society53</td>
<td>Preterm</td>
<td>I: Need for immediate resuscitation</td>
<td>CD: ≥30 s</td>
</tr>
<tr>
<td>2018</td>
<td>Confalonieri Ragonese Foundation with the Italian Society of Obstetrics and Gynecology51</td>
<td>Preterm singleton</td>
<td>M: Unstable conditions; multiple pregnancy</td>
<td>≥60 s and after the newborn has taken the first breath</td>
</tr>
<tr>
<td>2018</td>
<td>Italian Task Force for the Management of Umbilical Cord Clamping53</td>
<td>GA 34–36 wk</td>
<td>M: Massive uterine bleeding; CD under general anesthesia; collapse; cardiac arrest</td>
<td>CD: 30–60 s</td>
</tr>
<tr>
<td>2018</td>
<td>Italian Task Force for the Management of Umbilical Cord Clamping53</td>
<td>GA &lt;34 wk</td>
<td>I: Need for immediate resuscitation; birth asphyxia secondary to hypoxic-ischemic events; shoulder dystocia; twin-twin syndrome; rhesus disease; fetal hydrops; monochorionic twins</td>
<td>Position at or below the perineal level and</td>
</tr>
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</table>
in infants born at 23 to 27 weeks' gestation who received UCM. In their systematic review, Balasubramanian et al.\(^6\) also found significantly increased risk of severe IVH (grades 3 or higher) among preterm infants <34 weeks who received UCM compared with DCC in 4 RCTs. Importantly, the RCT by Katheria et al.\(^8\) which was the only included trial that found significantly increased risk, contributed nearly half the sample size of the UCM versus DCC comparison in this systematic review.\(^{69}\) Ongoing trials among infants of older gestational ages and follow-up studies on long-term neurodevelopmental outcomes will be important to support future recommendations on UCM.\(^{77,78}\)

Additionally, high-quality evidence on various cord milking techniques (eg, the number of milkings, speed of milking, and position of the infant) and studies on the outcomes of cord milking among infants needing resuscitation are needed.

Increased granularity of recommendations may improve health providers' ability and confidence in performing DCC. Only 4 statements were dedicated to DCC; all others embedded recommendations about DCC within broader topics. Guidelines focused on cord management would allow for specific recommendations for subpopulations (eg, various preterm gestational ages, modes of delivery). Further guidance is required on the position to hold the infant, the sequence of administration of uterotonic medications, temperature control, and other details. Additionally, DCC's life-saving benefits to extremely preterm and preterm infants\(^3\) should be noted as the basis of recommendations.

The language we use to discuss DCC may also encourage its practice and assist patients in understanding it as being a positive rather than a negative intervention. Among the 33 English-language statements, only 1 used the term “deferred cord clamping”\(^5\); all others referred to “delayed” or “late” cord clamping, which connote negativity and that immediate cord clamping is the norm.\(^12\) Hence, we recommend that

<table>
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<tr>
<td>2018</td>
<td>Italian Task Force for the Management of Umbilical Cord Clamping(^1)</td>
<td>Term</td>
<td>M: Massive uterine bleeding; CD under general anesthesia; collapse; cardiac arrest I: Need for immediate resuscitation; birth asphyxia secondary to hypoxic-ischemic events; shoulder dystocia; twin-twin syndrome; rheus disease; fetal hydrops; monochorionic twins UP: Doubt about integrity of umbilical cord; cord prolapse; uterine rupture; vasa previa; placental detachment; anamniotic embolism</td>
<td>Vaginal delivery: &gt;60 s, clamp by 3–5 min or until pulsation stops if requested by the mother</td>
</tr>
<tr>
<td>2018</td>
<td>SOGC(^6)</td>
<td>Term</td>
<td></td>
<td>Position: On mother’s abdomen or chest or below perineal plane CD 30–60 s (if &gt;60 s, ensure presence of neonatal resuscitation skills to evaluate fetomental transition)</td>
</tr>
<tr>
<td>2017</td>
<td>Queensland Clinical Guidelines(^6)</td>
<td>Term (GA 37–42 wk) born spontaneously in vertex position, and the mother and child in good condition</td>
<td>I: Heart rate &lt;60 beats per minute UP: Concern with cord integrity</td>
<td>Vaginal delivery: AMTSL: 1–3 min or until cord pulsation ceases; within 5 min if controlled cord traction anticipated PMTSL: After cord pulsation ceased or after birth of the placentas</td>
</tr>
<tr>
<td>2014</td>
<td>High Authority of Health (France)(^3)</td>
<td>Term</td>
<td></td>
<td>≥60s, do not delay management of an emergency</td>
</tr>
<tr>
<td>2014</td>
<td>NICE(^5)</td>
<td>Term (GA 37–42 wk)</td>
<td>I: Heart rate &lt;60 beats per minute, not getting faster UP: Concern with cord integrity</td>
<td>AMTSL: 1–5 min (clamp before 5 min to perform controlled cord traction. If the mother requests clamping later than 5 min, support her choice.) PMTSL: When cord pulsation has stopped</td>
</tr>
<tr>
<td>2019</td>
<td>Queensland Clinical Guidelines(^6)</td>
<td>Preventing and managing primary PPH</td>
<td></td>
<td>At risk of anemia due to fetomental alloimmunization: ≤30 s from birth, after first breaths if they are before 30 s</td>
</tr>
<tr>
<td>2018</td>
<td>Italian Task Force for the Management of Umbilical Cord Clamping(^1)</td>
<td>Dichorionic twins</td>
<td>M: Massive uterine bleeding; cesarean delivery under general anesthesia; collapse; cardiac arrest I: Need for immediate resuscitation; birth asphyxia secondary to hypoxic-ischemic events; shoulder dystocia; twin-twin syndrome; rheus disease; fetal hydrops; monochorionic twins UP: Doubt about integrity of umbilical cord; cord prolapse; uterine rupture; vasa previa; placental detachment; anamniotic embolism</td>
<td>At risk of anemia due to fetomental alloimmunization: ≤30 s from birth, after first breaths if they are before 30 s</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td>Other populations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FIGURE 4
(Continued).
future guidelines and studies use the more neutral term, “deferred.”

Although many professional societies advocate DCC for preterm and term infants, improved clarity and granularity can improve the quality of guidance on this issue. In this systematic review, we found that guidelines representing different professions within the same country provided different recommendations. For example, although the ACOG recommended deferring clamping for at least 30 to 60 seconds for term infants,24 the American College of Nurse-Midwives recommended deferring for up to 5 minutes for vaginally delivered term infants positioned skin to skin.25 Before its closure in 2018, the National Guideline Clearinghouse, an initiative of the US Department of Health and Human Services, allowed health providers to succinctly synthesize and compare guidelines on topics of interest to identify recommendations that are most suitable to their clinical setting and population. Our study provides this knowledge synthesis with the methodologic rigor of a systematic review and with quality appraisal of guidelines and recommendations. The abundance and heterogeneity of guidelines on placental transfusion emphasize the need for an updated resource for health providers that compiles and compares the content and quality of relevant statements.

To improve rates of DCC for infants born worldwide, strong guidelines should be amenable to adoption in everyday clinical settings. Among our included CPGs and other recommendation documents, 42% satisfactorily (domain score ≥50%) met the criteria within the AGREE-REX domain of implementability, which is used to assess the suitability of the recommendations for local adoption.20 In their systematic review of 10 studies conducted in high- and middle-income countries, Anton et al29 describe barriers to implementing placental transfusion in hospital settings. General challenges included staff unawareness and resistance to change, and pediatrician-specific concerns included uncertainty about the role of placental transfusion when neonatal resuscitation is needed and concerns about potential adverse outcomes, such as jaundice.29 Strategies to overcome barriers to implementation included education, creating protocols, auditing, providing constructive feedback, and improving multidisciplinary collaboration.29 For example, the CPG by NICE provides a modifiable clinical auditing tool for the third stage of labor.51 Additionally, joint guidelines by obstetrical and pediatric care providers and establishing of opportunities for multidisciplinary communication, such as a predelivery surgical pause and team debriefing, may facilitate improved rates of DCC. Beyond revealing the evidence-informed nature of DCC, efforts to address resistance to change and make DCC acceptable to policy-makers, health workers, and families will improve the rates of its adoption to practice.26 Although we found no country-specific recommendation statements produced in low-income countries, the WHO promotes the integration of DCC to national childbirth and postnatal care programming worldwide by employing strategies such as culturally

<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Population</th>
<th>Contraindications</th>
<th>Recommendations on DCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>The Royal College of Midwives24</td>
<td>Preterm and term</td>
<td>DCC is suggested but an optimal timing is not provided. Discuss DCC options with the mother in situations other than a vaginal delivery (instrumental, cesarean).</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Association of Ontario Midwives29</td>
<td>Preventing and managing PPH</td>
<td>DCC is recommended but an optimal timing is not provided.</td>
<td>AMTEL: Until cord pulsation ceases PPTSS: Until cord pulsation ceases or delivery of the placenta</td>
</tr>
<tr>
<td>2016</td>
<td>British Committee for Standards in Haematology30</td>
<td>Uncompromised infants</td>
<td>Need for resuscitation takes precedence</td>
<td>There is insufficient evidence to recommend an optimal timing.</td>
</tr>
<tr>
<td>2016</td>
<td>Resuscitation Council UK39</td>
<td>Uncompromised infants</td>
<td>Need for immediate resuscitation (there is insufficient evidence to recommend an optimal timing for severely compromised infants)</td>
<td>≥60 s</td>
</tr>
<tr>
<td>2015</td>
<td>SOGC39</td>
<td>Cord blood counseling, collection, banking</td>
<td>Cord blood collection should not interfere with DCC. Inform women and partners about the benefits of DCC and its impact on cord blood collection and banking.</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>Royal College of Obstetricians and Gynaecologists61</td>
<td>GA ≥23 wk, uncompromised infants after cord prolapse</td>
<td>Need for immediate resuscitation</td>
<td>DCC is recommended but an optimal timing not provided.</td>
</tr>
<tr>
<td>2014</td>
<td>WHO26,35</td>
<td>I: Asphyxiated and needs to be moved immediately for resuscitation (if there is experience providing effective positive pressure ventilation without cutting the cord, initiate ventilation before cutting the cord.)</td>
<td>≥60 s</td>
<td>DCC is recommended among women with HIV or women with unknown HIV status. Determine HIV status at birth and provide appropriate anti retroviral therapy.</td>
</tr>
<tr>
<td>2012</td>
<td>WHO41</td>
<td>I: Requiring positive pressure ventilation</td>
<td>Stimulation of infants who do not breathe spontaneously after drying by rubbing the back 2–3 times before clamping the cord and initiating positive pressure ventilation.</td>
<td>≥60 s</td>
</tr>
<tr>
<td>2014</td>
<td>WHO46</td>
<td>Preventing PPH</td>
<td>I: Asphyxiated and needs to be moved immediately for resuscitation</td>
<td>Vaginal and CD: Approximately 1–3 min after birth while providing essential newborn care; recommended among women with HIV or with unknown HIV status as well.</td>
</tr>
</tbody>
</table>

FIGURE 4
(Continued).
appropriate education on DCC, linking of implementation with other interventions (eg, improving women’s health literacy), and robust monitoring and evaluation.26

Birth brings together many disciplines; it is thus important that organizations guiding various disciplines are unified in their messages and use the current best evidence to provide detailed, comprehensive, and locally applicable recommendations so that change at the level of the birth can be implemented in a collaborative and sustainable way.10

CONCLUSIONS
In our systematic review of 44 CPGs and other recommendation statements, we found that professional maternal and infant health societies endorsed DCC to prevent neonatal morbidity and mortality among stable preterm and term infants. Only half the recommendations on the optional duration of DCC were supported by primary research or systematic review evidence, and in only 8% of statements was a mortality benefit of DCC for preterm infants reported. The current implementation of DCC may be increased with the provision of more unified, detailed, and evidence-based guidance on cord management.

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ABBREVIATIONS
ACOG: American College of Obstetricians and Gynecologists
AGREE: Appraisal of Guidelines for Research and Evaluation
AGREE II: Appraisal of Guidelines for Research and Evaluation II
AGREE-REX: Appraisal of Guidelines for Research and Evaluation Recommendation Excellence
CD: cesarean delivery
CPG: clinical practice guideline
DCC: deferred cord clamping
IVH: intraventricular hemorrhage
NICE: National Institute for Health and Care Excellence
RCT: randomized controlled trial
UCM: umbilical cord milking
WHO: World Health Organization

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Guidelines on Deferred Cord Clamping and Cord Milking: A Systematic Review
Sugee Korale Liyanage, Kiran Ninan and Sarah D. McDonald
Pediatrics 2020;146;
DOI: 10.1542/peds.2020-1429 originally published online October 21, 2020;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/146/5/e20201429

Data Supplement at:
http://pediatrics.aappublications.org/content/suppl/2020/10/20/peds.2020-1429.DCSupplemental