Systematic Review: The Clinical Effectiveness of Physiological (Expectant) Management of the Third Stage of Labor Following a Physiological Labor and Birth

Lesley Dixon, Judith T. Fullerton, Cecily Begley, Holly Powell Kennedy, and Karen Guilliland

BACKGROUND: The aim of this review was to establish the clinical effectiveness of physiological third-stage care following a physiological labor and birth.

METHODS: Seven databases and 9 journals were searched over a 25-year period resulting in the review of 38 papers. Of these, 34 papers were excluded because they included women who had received intervention during labor or birth; only 4 papers met the inclusion criteria. A research protocol and quality assessment were guided by the Centre for Reviews and Dissemination (CRD, 2008) and the meta-analysis of observational studies in epidemiology (MOOSE) guidelines for observational studies (Stroup et al., 2000). Studies were included if they described outcomes of care for women who had a physiological labor and birth and received expectant (physiological) care during the third stage of labor.

RESULTS: Two randomized controlled trials (RCTs) and 2 observational studies involving well, healthy women in high-income countries provided outcome information on a total of 35,455 participants and their third-stage outcomes. Results found little difference in mean blood loss between expectant third-stage care and active management (range 200–361 ml), no difference in maternal hemoglobin postnatal (when reported), and no increase in postpartum hemorrhage (PPH) when physiological care was provided.

KEY CONCLUSIONS AND IMPLICATIONS FOR PRACTICE: A physiological third stage of labor can be supported for women when there has been a physiological labor and birth, and the woman is well and healthy.

KEYWORDS: physiological third stage of labor; physiological birth; systematic review; blood loss; postpartum hemorrhage; retained placenta

INTRODUCTION

Global estimates of maternal deaths range from 342,900 (Hogan et al., 2010) to 358,000 annually (World Health Organization [WHO], United Nations Children’s Fund [UNICEF], United Nations Population Fund [UNFPA], & The World Bank 2010). Postpartum hemorrhage (PPH) accounts for approximately one quarter of these deaths and is a leading cause of maternal morbidity and mortality in the world (United States Agency for International Development [USAID], 2010). The International Confederation of Midwives (ICM) and the International Federation of Gynecology and Obstetrics (FIGO) have issued position statements on appropriate care for women during the third stage of labor to prevent PPH (ICM & FIGO, 2003, 2006). Active management of the
The third stage of labor (AMTSL) is recommended because it has been found to reduce the risk of hemorrhage of more than 1,000 ml in women of mixed levels of risk of hemorrhage in high-income countries (Begley et al., 2010). The main component of AMTSL is the use of a uterotonic drug, which may not be available to many women in low-income countries or settings or may not be acceptable for religious or other reasons (WHO, 2007a). The ICM/FIGO statements offer limited guidance for care of women who do not have access to a uterotonic (ICM & FIGO, 2003, 2006) during the third stage. Additionally, the use of uterotonic drugs, particularly those containing ergometrine, can cause side effects such as hypertension, pain, and increased rates of return to hospital in the postnatal period for bleeding (Begley et al., 2010). This may influence maternal preference to avoid uterotonic drugs if they are available, thus it is important to understand best practices and to examine outcomes during the third stage of labor when uterotonic drugs cannot, or have not, been used.

**Physiology of Labor, Birth, and the Third Stage of Labor**

Pregnancy, labor, and birth are the result of highly coordinated physiological interactions and signalling between neurons, neuroendocrines, endocrine, and immune cells (Douglas & Ludwig, 2008). The myometrial cells are thought to have an innate ability to contract with minimal external stimuli (Norwitz, Robinson, & Challis, 1999), and in late pregnancy (in what is now considered to be the activation stage), the oxytocin receptors in the myometrium increase 300-fold under the supportive influence of estrogen (Blackburn, 2007; Challis, Matthews, Gibb, & Lye, 2000). With the completion of the human genome project, there have been accelerated advances in understanding in many fields, especially neurophysiology. This field has identified how neurohormones facilitate an optimal internal environment and initiate adaptive physiological responses when necessary (Blackburn, 2007; Douglas & Ludwig, 2008; Lee, Macbeth, Pagani, & Young, 2009; Pert, 1997; Uvnäs-Moberg, Arn, & Magnusson, 2005). Neurohormones are hormones which are synthesized and released from neurons to work primarily within the brain; they also have a secondary function on different sites within the body. The body and mind are intricately linked through these neurohormones in a bidirectional network, in that what affects the mind/emotions can also affect the physiology of the body and vice versa (Pert, 1997). Oxytocin is a neurohormone and one of the prime initiators of rhythmic uterine contractions (Challis et al., 2000). It is released from the maternal hypothalamus in pulses during labor and the early postpartum period, resulting in the synchronous, high-amplitude uterine contractions necessary for parturition, which continue to be necessary during the third stage of labor (Fuchs et al., 1991). Oxytocin has other influences on emotion and physiology, specifically it regulates blood pressure, pulse, and body temperature; increases calmness; and alleviates pain (Lee et al., 2009; Uvnäs-Moberg, 2003).

It is now becoming clearer that interventions that have occurred during the first or second stages of labor can also affect the woman’s intrinsic physiology, which may continue to have an effect during the third stage of labor (Buckley, 2005; Odent, 1998). The prolonged infusion of intravenous oxytocin results in decreased uterine responsiveness because of the long-term loss of myometrial receptors (Phaneuf, Rodriguez Liñares, TambyRaja, Mackenzie, & López Bernal, 2000). Epidural analgesia during labor appears to result in lower plasma oxytocin levels, suggestive of interference in the labor physiology and normal oxytocin release (Rham, Hallgren, Högberg, Hurtig, & Odlind, 2002).

The third stage of labor begins following the birth of the baby and is completed following the separation and expulsion of the placenta and membranes and control of blood loss (National Collaborating Centre for Women’s and Children’s Health, 2007; Stables, 2000). Separation of the placenta commonly begins at the lower placental pole and proceeds upward (Mo & Rogers, 2008). The reducing size of the uterus, the reducing placental site, and gravity all assist with the separation of the placenta from the uterine wall. Bleeding is controlled by several concurrent mechanisms (Blackburn, 2007; Stables, 1999). Contraction and retraction of the myometrium occurs following expulsion of the placenta, followed by rapid hemostasis because of platelet activation and fibrin formation, which causes clotting at the placental site (Blackburn, 2007).

Uterine atony leading to PPH and retention of the placenta with a requirement for manual removal are two primary concerns during the third stage; both can result in maternal morbidity or mortality. PPH is defined as a blood loss of more than 500 ml with serious or severe PPH defined as a blood loss of more than 1,000 ml (WHO, 2009). It has also been suggested that any blood loss that results in physiological changes that threaten maternal health should be classified as a serious PPH (USAID, 2010). Factors that predispose for PPH include anemia, bleeding disorders, and multiple gestations. However,
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PPH can also occur in women who are considered to be at low risk, and influencing factors include abnormal uterine anatomy, placental abnormalities, or an overdistended uterus (Hastie & Fahy, 2009; Rogers et al., 1998). Grotegut, Paglia, Johnson, Thames, and James (2011) found that women with severe PPH had been exposed to significantly more oxytocin during labor when compared to matched controls. The underlying mechanism for this is thought to be a reduction in the sensitivity of the myometrial oxytocin receptors leading to uterine atony (Grotegut et al. 2011; Phaneuf et al., 2000).

Active Management of the Third Stage of Labor and Its Effects

Randomized controlled trials (RCTs) have been undertaken to test the efficiency of AMTSL, with the majority using definitions that included early cutting and clamping of the cord (Begley et al., 2010). The recently published Cochrane review found that the use of active management during the third stage not only reduced the risk of blood loss greater than 1,000 ml but also identified adverse side effects such as hypertension, pain, and increased rates of return to hospital in the postnatal period for bleeding (Begley et al., 2010). Some of these side effects may have been caused by inclusion of ergometrine as a component of the uterotic administered within the active management arm in three of the trials reviewed (Begley, 1990; Prendiville, Harding, Elbourne, & Stirrat, 1988; Thilaganathan, Cutner, Latimer, & Beard, 1993). However, in women at low risk of bleeding, no reduction or increase in severe blood loss (greater than 1,000 ml) was identified with active management of third stage, and the same adverse effects were still found (Begley et al., 2010). AMTSL has, however, been accepted into practice and is recommended in the form of professional or hospital guidelines in many countries (Ethiopian Society of Obstetricians and Gynecologists, 2005; NCC-WCH, 2007; Royal College of Obstetricians and Gynaecologists, 2002, 2009; WHO, 2007b).

Women giving birth in low-income countries have decreased access to hospital services and therefore are less likely to have interventions such as induction of labor, augmented labor, or epidural anesthesia (Derman et al., 2006; WHO, 2010b). They are also less likely to be able to access uterotonic medications following birth, whether the birth is in a hospital setting or at home because such drugs may be unavailable or the supplies are sporadic (Derman et al., 2006). Conversely, women in high-income countries may opt to forgo the uterotonic drug, and the NCC-WCH suggests that “women at low risk of postpartum haemorrhage who request physiological management of the third stage should be supported in their choice” (NCC-WCH, 2007, p. 21).

For women who have had a spontaneous labor and a normal birth (without intervention), it is reasonable to expect that the third stage will also follow a physiological pattern (Fry, 2007; Thorpe & Anderson, 2006). The research question arising from this initial review of the literature is “What are the outcomes of expectant (physiological) management of the third stage of labor following a physiological labor and birth?”

Context of This Review

This systematic review was undertaken to determine the outcomes of a physiological third stage following physiological first and second stages of labor and birth. It thus differs from the recently published Cochrane review (Begley et al., 2010) that examined active and physiological third stage management in all women, including those who had had interventions in the first and second stages. The intended outcome of the present review was to provide evidence to support and guide health practitioners, in particular midwives, providing care for women who choose this style of third-stage management or who have no access to uterotonsics and therefore have a physiological third stage by default.

METHOD

The primary objective of this systematic review was to assess the clinical effectiveness of physiological management for the third stage of labor following a physiological labor and birth. As part of setting up a review protocol and prior to commencing the review, it was necessary to clarify what was meant by “physiological labor and birth.”

Defining a Physiological Labor and Birth

The authors’ understanding of the concept of physiological birth was that it related to the characteristics of normal healthy functioning. For labor and birth, therefore, a definition was chosen in which there was minimal pharmaceutical interference in the way in which a woman’s body functioned during labor. Conceptualizing childbirth as physiological from start to finish was an
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Dixon et al. searched for further references. No language restrictions were applied so that all languages were considered and included in the search. All research studies published over the last 25 years were included. The primary search terms used were “expectant management” or “physiological management,” with the secondary search term being the “third stage of labor/birth.” Other search terms were “active management,” “placenta,” “hemorrhage,” “maternal death,” “anemia,” and “uterotonics.”

Data Extraction and Assessment Strategy

The search resulted in the identification and screening of 2,701 titles and abstracts. A total of 38 full texts were retrieved and assessed for eligibility using the data extraction tool with particular emphasis placed on inclusion and exclusion criteria (see Table 1). Studies were included if they had a description of expectant management; clear criteria for intervention or treatment; some demographic data such as age, ethnicity, and socioeconomic status; and outcome measures of health effects. Studies were excluded if they involved participants whose labor or birth could be considered nonphysiological such as induction of labor; augmentation with oxytocin during labor; and operative births such as forceps, ventouse, or cesarean section. Additionally, complex pregnancy issues such as preterm birth, multiple pregnancy, pregnancy-induced hypertension (PIH), antepartum hemorrhage (APH), vaginal birth after cesarean section, high reported levels of epidural anesthesia (greater than 50% of participants), and/or episiotomy (greater than 50% of participants) were also excluded because of the increased risk of PPH associated with these conditions. The controlled trials were assessed and analyzed for bias looking at randomization, performance bias, and data collection bias.

A meta-analysis was not an appropriate statistical approach because the studies selected for review included differing research approaches, including the use of observational data. There was therefore little homogeneity among the studies, which would have increased the risk of error in interpretation of meta-analytic data. Instead, the findings were synthesized through a narrative approach.

Excluded Studies

Thirty-eight studies that could have some relevance were identified and assessed against the research protocol of which 34 were excluded (Figure 1). Of the 38 identified
FIGURE 1 Flow chart of study selection process.
TABLE 1 Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>INCLUSION CRITERIA</th>
<th>EXCLUSION CRITERIA</th>
</tr>
</thead>
</table>
| Participants included who had a physiologically normal labor and included:  
  • >37 weeks pregnancy  
  • Singleton cephalic pregnancy  
  • Spontaneous labor and birth | Research studies excluded if there were any of the following interventions during labor or birth:  
  • Induction of labor  
  • Augmentation during labor  
  • Operative birth such as forceps, ventouse extraction, or cesarean section |
| The study has a description/explanation of expectant management style. | Research studies excluded if participants had any of the following:  
  • Preterm labor and birth  
  • Multiple pregnancy  
  • Pregnancy-induced hypertension  
  • Antepartum hemorrhage  
  • History of bleeding disorders |
| Study has a description/explanation of intervention/treatment such as active management. | Research studies excluded if participants had any of the following:  
  • Vaginal birth after cesarean section  
  • High reported levels of epidural anesthesia >50% of participants |
| Demographic data of the participants is included such as  
  • age,  
  • ethnicity, and  
  • socioeconomic status. | Research studies excluded if participants had any of the following:  
  • High reported levels of episiotomy >50% of participants |
| The study provides clear concise outcome data of health effects. | |

studies, 13 were RCTs that compared some form of expectant management or placebo given with AMTSL. Six of these RCTs were excluded because they included either instrumental births, induction of labor, or augmentation of labor (Begley, 1990; Giacalone et al., 2000; Khan, John, Wani, Doherty, & Sibai, 1997; Nordström, Fogelstam, Fridman, Larsson, & Rydhstroem, 1997; Prendiville et al., 1988; Rogers et al., 1998). A further four were excluded because of a lack of description of the expectant management arm of the trial, along with a lack of specific exclusion criteria for instrumental births, induction, and augmentation (Derman et al., 2006; Ecra et al., 2007; Jerbi, Hidar, Elmoueddeb, Chieb, & Khairi, 2007; Miller et al., 2009). One was excluded because intravenous syntocinon was commenced following physiological third stage (as part of a fourth stage), which was considered to be an intervention and therefore outside the search parameters (Kashanian, Fekrat, Masoomi, & Sheikh Ansari, 2010). Of the remaining 25 papers identified, 23 were excluded because they were either surveys of practice, discussion papers, or papers describing associated third-stage practice (see Table 2).

Included Studies

Four studies met all the inclusion criteria (see Table 3). Therefore, this review has included two controlled trials: one from the United Kingdom and one from Iran (Thilaganathan et al., 1993; Vasegh, Behryiaee, Mahmoodi, & Salehi, 2005), with a further two observational research studies: one from the Netherlands and one from New Zealand (Bais, Eskes, Pel, Bonsel, & Bleker, 2004; Dixon et al., 2009).

Analysis and Quality Assessment

The CRD guidelines for quality assessment for the RCTs and the MOOSE guidelines for observational studies were used to support analysis and quality assessment (Stroup et al., 2000). These were broadly related to study design, risk of bias, and the quality of reporting. Both of the controlled trials had small sample sizes, which reduced their power, and neither trial was able to blind the caregiver to the intervention or outcome assessment effectively, increasing the risk of allocation and performance bias. Thilaganathan et al. (1993) have clear inclusion/exclusion criteria and a clear description of active and physiological management but did not describe how they randomized their sample. Vasegh et al. (2005) describe how they selected their sample, but they used alternate allocation with odd and even numbers rather than random selection. They also provided a placebo during third-stage management in an attempt to blind caregivers to the intervention. However, because AMTSL includes other interventions as well as administration of a uterotonic, blinding cannot be successful. In addition, the researchers were also the caregivers (as midwives), increasing the risk of outcome bias. The original paper is written in Persian, and the English translation of their study description required careful
TABLE 2  Studies Excluded and Reasons for Exclusion

<table>
<thead>
<tr>
<th>REASON FOR EXCLUSION</th>
<th>NO</th>
<th>STUDY AUTHORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT of active and physiological management but participants were included who had an</td>
<td>4</td>
<td>Prendiville, Harding, Elbourne, &amp; Stirrat, 1988</td>
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<tr>
<td>induction and/or augmentation of labor</td>
<td></td>
<td>Begley, 1990</td>
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<td></td>
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<td>Nordström, Fogelstam, Fridman, Larsson, &amp; Rydhstroem, 1997</td>
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<td></td>
<td></td>
<td>Rogers et al., 1998</td>
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<tr>
<td>RCT of active and physiological management but participants were included who had</td>
<td>2</td>
<td>Khan, John, Wani, Doherty, &amp; Sibai, 1997</td>
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<tr>
<td>forceps and/or ventouse births and augmented labor</td>
<td></td>
<td>Giacalone et al, 2000</td>
</tr>
<tr>
<td>Expectant management description was that of active management (cord clamped and cut</td>
<td>1</td>
<td>Jerbi, Hidar, Elmoueddeb, Chaieb, &amp; Khairi, 2007</td>
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<tr>
<td>and CCT—the only difference in management was the provision or not of IV oxytocin</td>
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<td></td>
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<tr>
<td>Inclusion of preterm birth and no clear description of expectant care provision</td>
<td>1</td>
<td>Derman et al., 2006</td>
</tr>
<tr>
<td>No description or definition of expectant management within the research (one of</td>
<td>2</td>
<td>Ecra et al., 2007</td>
</tr>
<tr>
<td>which also had high levels of CCT</td>
<td></td>
<td>Miller et al., 2009</td>
</tr>
<tr>
<td>Intravenous syntocinon commenced following delivery of placenta (fourth stage)</td>
<td>1</td>
<td>Kashanian, Fekrat, Masoomi, &amp; Sheikh Ansari, 2010</td>
</tr>
<tr>
<td>Excluded as intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systematic reviews of existing papers</td>
<td>2</td>
<td>Gyte, 1994</td>
</tr>
<tr>
<td>Discussion papers about physiological/expectant management and active management</td>
<td>10</td>
<td>Prendiville, Elbourne, &amp; McDonald, 2009</td>
</tr>
<tr>
<td>Survey of practice and/or interpretation of third stage management</td>
<td>8</td>
<td>Brucker, 2001</td>
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<td></td>
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<td>Nothnagle &amp; Taylor, 2003</td>
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<td></td>
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<td>Lemay, 2004</td>
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<td></td>
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<td>Kanikosamy, 2007</td>
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<td>Fry, 2007</td>
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<td></td>
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<td>McDonald, 2007</td>
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<td></td>
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<td>Bair &amp; Williams, 2007</td>
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<td>Soltani, 2008</td>
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<td>Hastie &amp; Fahy, 2009</td>
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<td>Featherstone, 1999</td>
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<td>Festin et al., 2003</td>
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<td>Cherine et al., 2004</td>
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<td></td>
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<td>Armbruster, 2006</td>
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<td></td>
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<td>Winter et al., 2007</td>
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<td></td>
<td></td>
<td>Jangsten, Hellström, &amp; Berg, 2010</td>
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<td></td>
<td></td>
<td>Tan, Klein, Saxell, Shirkoothy, &amp; Asrat, 2008</td>
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<tr>
<td></td>
<td></td>
<td>Karolinski et al., 2009</td>
</tr>
<tr>
<td>Cord care/drainage and the third stage</td>
<td>1</td>
<td>Soltani, Dickinson, &amp; Symonds, 2005</td>
</tr>
<tr>
<td>Differing third stage care components with active management</td>
<td>2</td>
<td>Alhabe, Aleman, Tomasso, Gibbons, Vitureira, Belizan, &amp; Beukenks, 2009</td>
</tr>
<tr>
<td>Total studies excluded</td>
<td>34</td>
<td>Holmeyr, Abdel-Aleem, &amp; Abdel-Aleem, 2008</td>
</tr>
</tbody>
</table>

Note. RCT = randomized controlled trial; CCT = controlled cord traction; IV = intravenous.

reading and inter-reader agreement about the interpretation of the results.

The observational studies have provided descriptions of care along with outcomes of different management regimes. As such, there is an inherent bias because of the inability to randomize the samples and observe outcomes following control of the variables. The difference in culture, health care provision, and context of care between the two countries along with the different aims and study designs makes the interpretation and summary of these results problematic. Additionally, the results cannot prove a cause and effect because any additional confounding variables may not have been accounted for. However, the New Zealand study has described third-stage outcomes after physiological management for one of the largest cohorts of women globally to date (Dixon et al., 2009).
### TABLE 3  Studies Included in Systematic Review

<table>
<thead>
<tr>
<th>PLACE, AUTHOR, AND YEAR</th>
<th>STUDY AIM AND DESIGN</th>
<th>PARTICIPANTS—INCLUSION AND EXCLUSION CRITERIA</th>
<th>EXPECTANT/INTERVENTIONS MANagements DESCRIBED</th>
<th>KEY FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom; Thilaganathan, Cutner, Latimer, &amp; Beard, 1993</td>
<td>RCT—using randomization tables—no description of randomization method</td>
<td>193 women admitted to hospital in spontaneous labor between 37–42 weeks. Exclusions: • Augmented labor • Operative births • Third-degree tear • Cervical lacerations</td>
<td>AMTSL: • 1 ml Syntometrine IM soon as baby is born • Cord immediately clamped and cut • Placenta delivered by CCT Expectant care: • Cord not cut or clamped • Observe for signs of placental separation; • At which point mother encouraged to adopt an erect position • Maternal effort to facilitate placental birth</td>
<td>Blood Loss No significant difference in blood loss between 2 groups ( p &gt; .5 ) Mean EBL: 200 ml in both groups Maternal Hb Fall in postnatal Hb: 0.5 (AMTSL) vs. 0.7 (Expect) Length of third stage of labor Longer third stage for physiological group ( p &lt; .001 )</td>
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<tr>
<td>Iran; Vasegh, Behyriayee, Mahmoodoy, &amp; Salehi, 2005</td>
<td>Controlled trial allocated quasi-randomly by use of alternate numbers into two groups of 47</td>
<td>94 participants between 37–43 weeks pregnancy with live single cephalic fetus and Hb &gt;10 g/dl Exclusions: • APH • Previous PPH • Previous LSCS • Raised blood pressure • Diabetes • Liver disease • Blood clotting issue • IOL • Augmented labor</td>
<td>AMTSL: • 10 IU Syntocinon after birth of baby • Cord cut and clamped immediately • Placenta delivered by Brandt-Andrews method Expectant care: • Injection of distilled water • Cord not clamped or cut until pulsation ceased • Placenta delivered by a gentle pull from birth attendant and maternal effort In both groups, the mothers’ position was on her back.</td>
<td>Blood loss Blood loss volumes not defined Maternal Hb No statistical differences between groups Length of third stage of labor Length of third stage mean: 9 min (AMTSL) vs. 13 min (expect) PPH Heavy PPH occurred for one woman in each group—but no definition of heavy PPH</td>
</tr>
</tbody>
</table>
The Netherlands; Bais, Eskes, Pel, Bonsel, & Bleker, 2004

To determine the incidence and risk factors for standard and severe postpartum hemorrhage

Population-based cohort study; An unselected cohort of nulliparous women from the Zaanstreek district of the Netherlands

Risk stratification is part of routine care; midwives provide care for all women with low-risk pregnancies.

3,464 nulliparous women of which 1,416 were described as low risk, which included
- Women with an uneventful pregnancy
- First and second stage of labor (low risk)
- Choice of home or hospital birth

AMTSL:
- 5 or 10 IU of oxytocin after the birth of the baby
- Early cord clamping was only done in cases of nuchal cord or fetal distress.
- After signs of separation, the placenta was delivered by maternal effort aided by suprapubic pressure without CCT.

Expectant care:
- As discussed previously but without administration of oxytocic drug
- Oxytocic given at the discretion of the midwife or obstetrician providing care

For low-risk group, 50% given oxytocin prophylactically.

Blood loss
Blood loss not significantly different between groups

Maternal Hb
Not measured

Length of third stage of labor
A prolonged third stage implicated in increased PPH or retained placenta.

PPH
Severe PPH was 4.0% for low-risk group but not stratified between groups.

Retained placenta
Retained placenta 1.2% for low risk group—not stratified between groups.

New Zealand; Dixon, Fletcher, Tracy, Guilliland, Pairman, & Hendry, 2009

To explore the third stage of labor care practices of midwives in New Zealand.

Population-based cohort study reviewing care and outcomes for 33,752 over a 5-year period.

16,238 women (expect)
17,514 women (AMTSL)

Inclusion criteria:
- Spontaneous vaginal birth
- >37 weeks completed pregnancy

Exclusion criteria:
- Previous PPH
- Previous cesarean section
- Multiple pregnancy
- Breech birth
- Intrauterine death
- Operative birth
- IOL
- Augmented labor

The type of third stage care was defined and recorded by the midwife at time of care provision.

The professional guidelines definitions:

AMTSL
- Uterotonic drug given as soon as possible after birth or with the anterior shoulder.
- Cord clamped and cut
- CCT

Expectant care
- No uterotonic drug given.
- Delayed clamping or cutting of cord for several minutes or until placenta is expelled.
- Once there are signs of separation encourage upright position and maternal effort to expel placenta

Blood loss
Less blood loss in expect group; Mean blood loss: 213.6 (expect) vs. 241.6 (AMTSL) (p < .0001)

Maternal Hb
Not measured

Length of third stage of labor
Length of third stage: >40 minutes for 11.3% of physiological care group but no increase in PPH

PPH
>500 ml: 3.6% (expect) vs. 6.8% (AMTSL)
>1,000 ml: 0.6% (expect) vs. 1.5% (AMTSL) (p < .001)

Retained placenta
0.2% (expect) vs. 0.7% (AMTSL)

Note: RCT = randomized controlled trial; AMTSL = active management of third stage of labor; IM = intramuscular injection; CCT = controlled cord traction; EBL = estimated blood loss; Hb = hemoglobin; Expect = expectant or physiological management; APH = antepartum hemorrhage; PPH = postpartum hemorrhage; LSCS = lower segment caesarean section; IOL = induction of labor.
**FINDINGS**

**Controlled Trials**

The two controlled trials compared outcomes between physiological (expectant) and active management for the third stage (Thilaganathan et al., 1993; Vasegh et al., 2005). Both trials had extensive exclusion criterion, which ensured that the participants could be described as having had a physiological labor and birth when randomized to physiological or active third-stage management. Descriptions of expectant management were clear and detailed in the U.K. trial (Thilaganathan et al., 1993) but were less detailed in the Iranian trial (Vasegh et al., 2005). Vasegh et al. (2005) described giving a placebo instead of oxytocin, with the cord not clamped or cut until pulsation ceased. The placenta was delivered by gentle pulling and maternal effort.

**Observational Studies**

The Dutch study (Bais et al., 2004) provided information on 3,464 nulliparous women and stratified for high and low risk factors. This was a descriptive study to determine the incidence and risk factors for PPH in nulliparous women giving birth vaginally. The number stratified as low risk was 1,416 (41% of the overall sample) (Bais et al.). Nearly 50% of women in the low-risk group received prophylactic oxytocin during the third stage (described as active management) with a similar number receiving physiological management.

The New Zealand College of Midwives (NZCOM) study (Dixon et al., 2009) reported on the care provided by midwives during the third stage. This was a descriptive study of 33,752 women who gave birth over a 5-year period and were stratified to ensure that a physiologically normal labor and birth had occurred. Midwives in New Zealand provide both active and physiological management for the third stage, following discussion and informed decision making with the woman. Nearly half (48.1%) of the women in the New Zealand study had a physiological third stage with 51.9% having an actively managed third stage. Extensive inclusion/exclusion criteria were applied to remove antenatal risk factors for PPH and interventions during labor such as induction, augmentation of labor, and/or instrumental and operative births (Dixon et al., 2009).

The manner of management of the third stage in the Netherlands study was determined by the midwife or obstetrician providing care (Bais et al., 2004). Expectant third-stage management was described as the placenta being expelled with maternal effort after signs of separation and aided by suprapubic pressure but without controlled cord traction (this is a similar description to physiological management). Early cord clamping occurred only when there was fetal distress or a nuchal cord. Active management was described as the giving of prophylactic oxytocin (5 or 10 IU) after the birth of the baby with the same management as described previously. Therefore, the only difference between active and physiological management was the giving of a uterotonic after the birth of the baby and prior to the placenta being expelled (which is not in exact compliance with the AMTSL protocol). In the New Zealand study, the management of the third stage was determined by the midwife providing care and defined as either physiological or active with associated uterotonnic drug provision (Dixon et al., 2009).

**Outcome Measures**

None of the included studies provided outcomes for maternal views, economic outcomes, or neonatal clinical outcomes, and therefore subgroup analyses could not be performed for these variables. Outcomes that were reported for some or all of the studies were blood loss, maternal hemoglobin measurement, length of third stage, PPH, and retained placenta, and these are reported next and summarized in Table 3.

**Blood Loss**

Visual estimation of blood loss is considered to be inaccurate although it remains one of the most commonly used ways of assessing blood loss in practice (Glover, 2003; Kavle et al., 2006; Razvi, Chua, Arulkumaran, & Ratnam, 1996; Schorn, 2010). Both controlled trials reported no statistical differences when comparing blood loss between the active and physiological arms of the trial (Thilaganathan et al., 1993; Vasegh, 2005). The blood loss was estimated in the U.K. study and was documented as a mean of exactly 200 ml in each study group (Thilaganathan et al., 1993). Vasegh et al. (2005) do not describe whether the blood loss variables were measured or estimated and do not provide information on blood loss volumes. For the Dutch observational study, the blood loss was a combination of measured and estimated blood loss (Bais et al., 2004), whereas the New Zealand study was based on estimated blood loss (Dixon et al., 2009).

The Dutch study found that the blood loss was not significantly different between those women who received prophylactic oxytocin and those that did not
(\(p = .8\)) (Bais et al., 2004). Blood loss was both measured and estimated, and the mean blood loss was 361 ml for both groups (Bais et al., 2004). For the New Zealand study, blood loss was estimated; study findings indicated that women who had a physiological third stage had less blood loss than those who were actively managed with a mean blood loss of 213.6 ml (CI 211.6–215.5) for the physiological group and 241.6 ml (CI 239.4–243.8) for the active management group (\(p < .0001\)) (Dixon et al., 2009).

### Maternal Hemoglobin

Both controlled trials measured changes in hemoglobin levels (Thilaganathan et al., 1993; Vasegh et al., 2005). Vasegh et al. (2005) measured hemoglobin and hematocrit before birth and 24 hours following the birth, whereas Thilaganathan et al. (1993) measured hemoglobin on admission to the labor ward and on the third postpartum day. Both found that although there was a fall in hemoglobin postnatally, these differences were not statistically significant between the expectant and active management groups. Neither of the observational studies (Bais et al., 2004; Dixon et al., 2009) reported on this measure.

### Length of Third Stage of Labor

Both controlled trials found that expectant management resulted in a longer third stage (Thilaganathan et al., 1993; Vasegh et al., 2005). The U.K. trial found that there was a statistically significant difference in the length of the third stage with expectant third stage longer than the actively managed third stage (13 minutes physiological to 6 minutes active \(p < .001\)) (Thilaganathan et al., 1993), whereas Vasegh et al. (2005) found a longer third stage, but the difference did not reach statistical significance. Of the observational studies, the Dutch study found that longer duration of third stage increased the risk of severe PPH (7.1% OR 3.6), and the authors concluded that a longer third stage of more than 30 minutes was a significant risk factor for PPH; however, they did not stratify to active or expectant management for this aspect (Bais et al., 2004). The New Zealand study found that a physiological third stage was longer than an actively managed third stage (66.3% took more than 10 minutes in the expectant group compared with 70% taking less than 10 minutes in the active group) but did not increase the incidence of PPH (Dixon et al., 2009).

### Postpartum Hemorrhage and Blood Transfusion

Vasegh et al. (2005) reported that 4 (8.5%) out of 47 in the actively managed group had a PPH compared with 7 (14.8%) out of 47 in the physiologically managed group, although the definition of PPH was not provided. These numbers are too small to provide adequate power to assess any statistically significant difference. The U.K. study (Thilaganathan et al., 1993) did not report on PPH. The Dutch study reported the incidence of severe PPH (blood loss exceeding 1,000 ml) to be 4.0% in the low-risk group compared to 4.2% in the full cohort with a red cell transfusion received by 1.8% of the women who had a severe PPH (Bais et al., 2004). For the New Zealand study, the PPH rate for the whole cohort was 5.3% (Dixon et al., 2009). When stratified for active and physiological management, the incidence of PPH (blood loss >500 ml) was 6.8% for women who were actively managed, of which 1.5% had a blood loss of more than 1,000 ml. For those that had no uterotonic (expectant management), 3.7% had a blood loss of more than 500 ml, of which 0.6% had a blood loss of more than 1,000 ml (Dixon et al., 2009). The New Zealand study did not have information on the number of blood transfusions administered.

### The Need for Treatment and Outcomes

A need for treatment was clarified in the New Zealand research, which discussed timing of administration of the uterotonic as either prophylaxis or treatment (Dixon et al., 2009). Comparisons were made between physiological management and treatment versus active management and further treatment. Results demonstrated a higher need for treatment during a physiological third stage (13.2% physiological to 6.9% active management \(RR 1.7, CI 1.6–1.8\)) but less PPH (3.7% physiological to 6.9% active, \(RR 0.54, CI 0.5–0.6\)) for the physiological group.

### Retained Placenta

Both of the controlled trials provided data on retained placenta but—because of the small sample size—lacked the power to provide statistical significance (Thilaganathan et al., 1993; Vasegh et al., 2005). The incidence of retained placenta was 1.2% for the Dutch cohort but lacked stratification into expectant or active management groups (Bais et al., 2004). The incidence of manual removal of retained placenta was 0.2% for the
physiological management group and 0.7% (p < .0001) for the actively managed cohort in the New Zealand study (Dixon et al., 2009).

DISCUSSION

The aim of this systematic review was to determine the most effective management during the third stage when there are no uterotonics given due to availability or choice. There is increasing evidence that intervention during the first or second stages of labor may increase blood loss during the third stage (Buckley, 2005; Grotegut et al., 2011; Phaneuf et al., 2000; Rham et al., 2002). Many midwives practice from a philosophy that argues that a physiological third stage is a logical conclusion to a physiological labor and birth (Fry, 2007; NZCOM, 2006; Thorpe & Anderson, 2006). So, when assessing the clinical effectiveness of physiological management for the third stage of labor, it was necessary to specify that labor and birth were also physiological throughout. The very few studies undertaken on the physiology of the third stage of labor over 25 years is surprising. This concept of no pharmaceutical interference at any stage of the labor was unique and has not been recognized as important in many of the research studies comparing third-stage outcomes. It has led to exclusion of most research trials on the subject and has therefore considerably reduced the number of RCTs that could be included in this review. The two RCTs included were small in size, which limits their power to provide statistically significant results (Thilaganathan et al., 1993; Vasegh et al., 2005). The inclusion of two large observational studies has, however, provided support for the findings of the two small RCTs (Bais et al., 2004; Dixon et al., 2009).

The review has explored the benefits and risks of a physiological third stage. It found that although the measurement of blood loss was a subjective measure for all of the included studies, the results suggest minimal differences in blood loss volumes or PPH rates (when reported) when compared to an actively managed third stage. Although a longer third stage of labor was found more likely with physiological management, three of the studies reported no increase in the blood loss volume or PPH rates (Dixon et al., 2009; Thilaganathan et al., 1993; Vasegh et al., 2005). Overall, the reporting levels of retained placenta or requirement for blood transfusion were low and when reported, did not achieve statistically significant differences. Measurement of hemoglobin was undertaken in the two controlled trials (Thilaganathan et al., 1993; Vasegh et al., 2005), and there were no statistically significant differences in outcomes.

There appeared to be an increased requirement for treatment with a uterotonic in the physiological group when compared to the active group, but this did not result in increased blood loss or PPH rates (Dixon et al., 2009; Thilaganathan et al., 1993). Similar findings were reported in two recently published double-blind randomized noninferiority trials, undertaken in five low-income countries (Blum et al., 2010; Winikoff et al., 2010). These studies were undertaken to establish whether misoprostol was as effective a treatment for PPH as oxytocin. The results found that treatment (with either oxytocin or misoprostol) is more effective and acts more quickly when the woman has not previously been exposed to oxytocin during labor for induction or augmentation or given oxytocin prophylactically for the third stage. This suggests that when a uterotonic is given as a treatment, it is more effective at promoting the cessation of bleeding than when it has previously been given as a prophylactic.

All of the included studies were undertaken in high-income countries, where it can be presumed there is easy access to uterotonics if required, and the women were assumed to be healthy. In many low-income countries, births occur at home or in a community health setting, where there is often limited access to health professionals or uterotonic drugs (WHO, 2010). It is recognized that women in low-income countries may not be healthy, and there is potential for labor to be physiologically compromised because of anemia, HIV, or other conditions. However, until there is an improved understanding of the outcomes for the healthy physiological third stage, there cannot begin to be an understanding of what changes should be made for those who are less healthy and whose parturition is not physiological. For example, the finding that uterotonics may act better if used as a treatment rather than a prophylactic needs exploring because it has implications for some low-income countries where a rapid response is compromised by lack of access to emergency referral services.

A trend is noted for research trials (excluded from this review because of interventions in labor) investigating placebo versus oxytocin or misoprostol administration in low-income countries to include the additional currently recommended components of active management (controlled cord traction and fundal massage) within the placebo arms, despite the lack of administration of a uterotonic (Jerbi et al., 2007; Miller et al., 2009). This offers a benefit to the blinding of the study but introduces a new question about which components of third-stage management are protective against PPH.
There is a need for additional large RCTs to study prospectively the components of physiological third stage of labor and outcomes for women who have had a physiological labor and birth. Further, RCTs are also required to ascertain whether or not exposure to oxytocin during labor and birth, or instrumental birth, cause an increased risk of PPH. Any future research that explores third-stage management outcomes should include a full description of the management components provided during the third stage (such as time to uterotonic administration if any, time of cord clamping, position of woman, and time to birth of placenta), the need for treatment with a uterotonic if considered necessary by the health professional (usually midwife), and a description of how the blood loss measurement has been made or estimated. Additional important outcome measures include the need for blood transfusion or blood products, retention of placenta, PPH measurement, neonatal outcomes, and maternal views.

CONCLUSION

The findings of this systematic review based on mainly observational data indicate that when physiological labor and birth occurs, there is no increase in blood loss or PPH when physiological management is provided for the third stage. Further, rigorous RCTs are necessary to test this hypothesis but, as a guide to care in the meantime, it would appear that the use of physiological third-stage management can be supported as a choice for healthy women who have had a physiological labor and birth. Given the documented risks of active management and the demonstrated effectiveness of uterotonic treatment when given following a physiological labor and birth, it would appear that this recommendation provides the optimum care for low-risk women. This information should be provided to women at low risk to PPH so that they may make an informed choice.

Because all studies included in this review were conducted in high-income countries, most women were likely to be healthy. The findings and conclusion cannot, therefore, be applied to compromised populations of pregnant women.

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