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## Outcome measures in studies on the use of oxytocin for the treatment of delay in labour: A systematic review

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## ABSTRACT

**Objectives:** to identify primary and secondary outcome measures in randomised trials, and systematic reviews of randomised trials, measuring effectiveness of oxytocin for treatment of delay in the first and second stages of labour, and to identify any positive health-focussed outcomes used.

**Design:** eight relevant citation databases were searched up to January 2013 for all randomised trials, and systematic reviews of randomised trials, measuring effectiveness of oxytocin for treatment of delay in labour. Trials of active management of labour or partogram action lines were excluded. 1918 citations were identified. Two reviewers reviewed all citations and extracted data. Twenty-six individual trials and five systematic reviews were included. Primary and secondary outcome measures were documented and analysed using frequency distributions.

**Findings:** most frequent primary outcomes were caesarean section ( $n=15$ , 46%), length of labour ( $n=14$ , 42%), measurements of uterine activity ( $n=13$ , 39%) and mode of vaginal birth ( $n=9$ , 27%). Maternal satisfaction was identified *a priori* by one review and included as a secondary outcome by three papers. No further positive health-focussed outcomes were identified.

**Key conclusions:** outcomes used to measure the effectiveness of oxytocin for treatment of delay in labour are heterogeneous and tend to focus on adverse events.

**Implications for practice:** it is recommended that, in future randomised trials of oxytocin use for delay in labour, some women-centred and health-focussed outcome measures should be used, which may instil a more salutogenic culture in childbirth.

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## Introduction

Labour duration has shown a wide variation in different women (Albers, 1999; Vahratian et al., 2006; Neal et al., 2010), and slow labour progress is common in nulliparous women. It is associated with childbirth complications, concerns for fetal well-being, and negative birth experiences (Waldenström et al., 2004), and is one of the main indications for unplanned caesarean section in labour (Bugg et al., 2006; Florica et al., 2006).

Some evidence indicates that early oxytocin administration is associated with an increase in spontaneous vaginal birth (Wei et al., 2009) but others conclude that oxytocin does not affect delivery mode (Bugg et al., 2013). Likewise, there is no consensus regarding doses of oxytocin (Xenakis et al., 1995; Oscarsson et al., 2006; Hayes and Weinstein, 2008). Systematic reviews of high versus low dose oxytocin for augmentation of delayed labour report shorter labour duration and an increase in spontaneous vaginal birth associated with high doses (Wei et al., 2010; Mori et al., 2011) but there are few studies and, overall, the evidence is scarce (Mori et al., 2011). This would appear to indicate that further research should be conducted, and therefore the outcome measures chosen should receive some attention.

Healthy outcomes and positive experiences are core issues for women in childbirth, yet the majority of outcome measures used in research are focussed on physical aspects only and refer to adverse outcomes (for example, pain requiring analgesia, admission to Special Care Baby Unit (SCBU), mortality). There is a need for inclusion of positive health-focussed outcome measures using a salutogenic approach. Salutogenesis concentrates on health and how it can be promoted, rather than focussing on illness and how it can be cured (Day-Stirk and Palmer, 2003), which is in congruence with the philosophy of childbirth that views pregnancy as a normal physiological event, not an illness. Smith et al. (2014), in a systematic review of 102 systematic reviews of maternity care, identified 16 categories of outcomes that could be called 'salutogenic'; these included mobility during labour, comfort, spontaneous rupture of membranes, intact perineum, well-being, and positive relationship with infant. Focussing on such outcomes may encourage clinicians to try to increase their incidence, thus improving care for mothers and infants.

Some positive outcomes are expected from oxytocin (e.g. shorter labour duration, spontaneous vaginal birth), but it is acknowledged as not only a powerful and effective drug (Clark et al., 2009; Rooks, 2009) but also one that is associated with adverse neonatal outcome and operative delivery (Bugg et al., 2006; Oscarsson et al., 2006). There is little evidence on the general impact of oxytocin during delay of labour, except that it shortens labour (Wei et al., 2009; Bugg et al., 2013; Mori et al., 2011). A good maternal and fetal outcome is the overall aim for

each labour and birth. However, comparisons between studies are challenging due to inconsistencies in choice, and definitions, of outcome variables, which indicates the need to develop a core set of outcomes (Devane et al., 2007). It remains unclear how, or if, the outcomes identified by Devane et al. (2007) (including maternal mortality, caesarean section rates, length of labour, analgesia, mode of vaginal birth, post partum haemorrhage, blood transfusion, Apgar scores, admission to SCBU, perinatal mortality or morbidity), and other more positive health-focussed outcomes, have been picked up in the light of the ongoing research on oxytocin during delay in labour.

This systematic review aims to identify primary and secondary outcome measures in randomised trials, and systematic reviews of randomised trials, measuring effectiveness of oxytocin for treatment of delay in the first and second stages of labour. The review will also identify any positive health-focussed outcome measures used in this field.

## Methods

Two of the authors performed a systematic search in March 2011, which was updated in January 2013, using the following databases:

- Maternity and Infant Care (MIDIRS).
- Cochrane Database of Systematic Reviews (CDSR).
- Cochrane Central Register of Controlled Trials (CENTRAL).
- Medical Literature Analysis and Retrieval System Online (MEDLINE).
- The Cumulative Index to Nursing and Allied Health Literature (CINAHL).
- Excerpta Medica Database (EMBASE).
- Database of Abstracts of Reviews of Effects (DARES).
- Health Technology Assessment Database.

A detailed search strategy was developed and tested for each database, restricted to English language publications. Appropriate keywords were combined with the Boolean operands 'and' and 'or' as appropriate; for example, for a search in MEDLINE, 'delay OR delayed OR progress\* OR augment\* OR dystoc\* OR slow OR arrested OR latent OR prolonged OR protracted OR active management OR partogram OR timing.' We also hand-searched the reference lists of all eligible studies for references to other possibly relevant studies. A flow diagram was produced (Fig. 1) to represent our search technique and results in accordance with the PRISMA statement (Liberati et al., 2009).

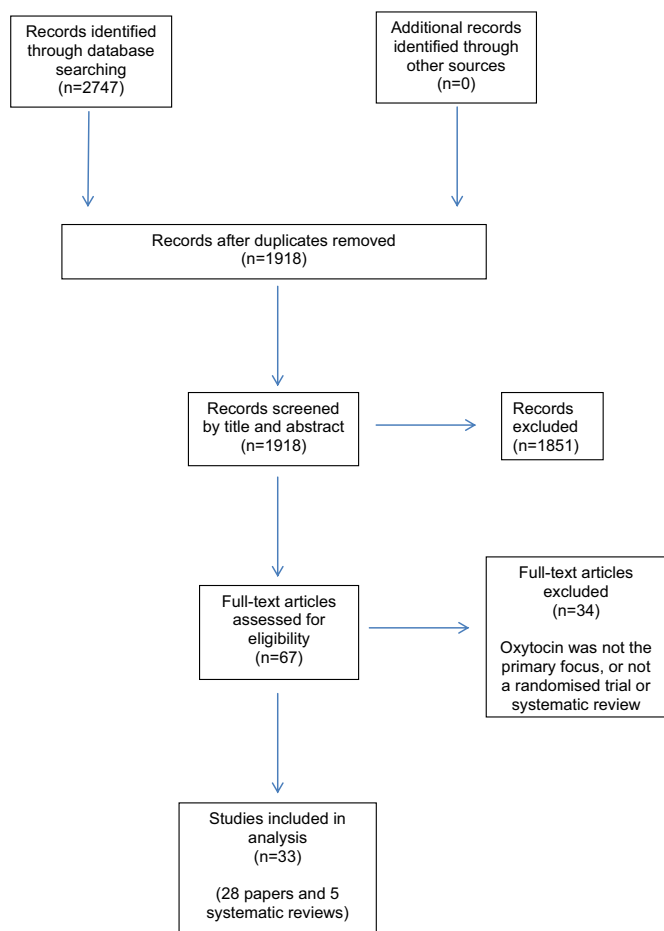


Fig. 1. Flow diagram of systematic review search.

### Eligibility criteria

We included randomised controlled trials (RCTs), and systematic reviews of RCTs. All studies used oxytocin for the treatment of delay in the first and second stage of labour as defined by the trial authors (e.g. delay of labour, slow progress for labour, prolonged labour, prolonged latent labour, late timing, diagnosis of arrested labour, no cervical change for two hours, no descent of the head). We excluded studies that compared the use of different partogram action lines, as the main focus was not on oxytocin. Studies that evaluated the use of active management of labour were also excluded, because these studies applied a package of care, which would have influenced the outcomes chosen.

### Data collection and analysis

Our search identified 1918 citations after removal of duplicates, of which 1885 were excluded. Each identified citation was reviewed independently by all review authors, working in pairs, and filtered through three screening levels i.e., (i) title screening (ii) title and abstract screening and (iii) full-text screening. Disagreement at any level was resolved through discussion between two reviewers with recourse to a third reviewer if required.

There were a number of papers where it was difficult to reach a decision as to whether the study looked at Active Management of Labour (AML), which was to be excluded, or oxytocin used for treatment of delay, which should be included. For example, Cohen et al.'s paper (1987) was eventually excluded, after much discussion. The authors said 'all subjects demonstrated an inadequate

pattern defined as a frequency of less than three contractions lasting 40 seconds each in a 10-minute time period' (p. 1175), which could have indicated delay, or perhaps just the latent phase of labour. As 'the early aggressive management protocol' was instituted 'within 30 minutes of admission to the labour ward' it seemed to be more like AML than waiting and eventually diagnosing delay in labour, therefore it was thought reasonable to judge this study as outside the scope of the review.

We finally included 28 papers, on 26 studies, for which data were extracted (Fig. 1). All papers except Sharami et al. (2012) were available as full text papers, and all provided an abstract. More recent papers had structured abstracts but this was less the case if the papers were published earlier. Two papers reported on different aspects of the same study (Bidgood and Steer, 1987a, 1987b) and one paper (Bergqvist et al., 2012) reported on a subsample of the study reported by Dencker et al. (2009). All included original studies ( $n=26$ ) were randomised controlled trials where at least one of the groups received oxytocin for augmentation for delay in spontaneous labour (Table 1).

Five systematic reviews of randomised trials were also included. In the five reviews there was a total of 45 included trials but several of these were already included in our review as individual studies, and many were included several times as they occurred in more than one review. The reviews included both randomised (and quasi randomised) trials, and both published and unpublished studies (Table 2). No quality assessment was made of selected papers and reviews, as only outcomes were to be counted, not results. Similarly, results are not included in the tables, as the focus is on outcomes measured.

Data were collected into a pre-prepared form by three authors and checked by three others. We counted all maternal and fetal outcomes used in the RCTs or specified *a priori* as outcomes in the reviews, and presented them as frequencies. Not all studies distinguished between primary and secondary outcomes. For the purposes of this review, outcomes were deemed to be 'primary' when the study authors presented them as such, or used a small number of outcomes in the power computation for sample size calculations. Other outcomes were then deemed to be 'secondary' (Table 3). When a study presented a large number of outcomes without distinguishing between primary and secondary, they were all deemed to be secondary outcomes. Positive health focussed-outcomes, defined as outcomes tending toward the health, rather than pathological, end of the health continuum (e.g. spontaneous birth, intact perineum, breast feeding), and women-centred outcomes such as maternal satisfaction, were also noted.

## Findings

### Description of included original studies

#### Demographic characteristics

Most of the trials (25 out of 26) included nulliparous women with a single cephalic pregnancy (Table 1). Eleven of these trials included both nulliparous and multiparous women. Only one study also included women with multiple pregnancies (Merrill and Zlatnik, 1999). One study differed from the others and included only women with previous caesareans and 'unknown' scars (Grubb et al., 1996). Women were most often randomised in the first stage of active labour but sometimes in early labour or in the second stage. Two studies (Saunders et al., 1989; Shennan et al., 1995) included only women using epidural analgesia. All trials included women at term and some studies also included women at an earlier gestational age (Table 1).

Various exclusion criteria were defined. Several studies stated fetal related exclusion criteria as signs of 'fetal distress', estimated

**Table 1**  
Characteristics and inclusion criteria of included RCTs.

| Reference                        | Country        | Total number of participants randomised             | Oxytocin group                                      | Comparison group   | Nulli-parous women | Multiparous women | Stage when randomised     | Comment                             |
|----------------------------------|----------------|---|---|--|--------------------|-------------------|---------------------------|-------------------------------------|
| Arulkumaran et al. (1989)        | Singapore      | 68 (34/34)  | Oxytocin until target uterine activity was achieved | Oxytocin until target uterine frequency was achieved                                 | Y                  |                   | Active labour             |                                     |
| Bergqvist et al. (2012)          | Sweden         | 536 (284/252) (sub-sample of Dencker et al. (2009)) | Oxytocin within 20 minutes                          | Expectancy three hours   | Y                  |                   | 4–9 cm                    |                                     |
| Bidgood and Steer (1987a, 1987b) | United Kingdom | 60 (21/19/20) (three arms)                          | Oxytocin low dose/high dose                         | Expectancy eight hours   | Y                  |                   | First stage active labour |                                     |
| Blanch et al. (2005)             | United Kingdom | 60 (21/20/19) (three arms)                          | ARM + oxytocin immediately/ARM only                 | Expectancy   | Y                  | Y                 | Active labour             |                                     |
| Bleich et al. (2011)             | USA            | 350 (174/176)                                       | Oxytocin  | Misoprostol  | Y                  |                   | 4–8 cm                    |                                     |
| Cluett et al. (2001)             | United Kingdom | 12 (4/4/4)  | Oxytocin  | Water birth pool or conservative management  | Y                  |                   | > 3 cm                    |                                     |
| Cluett et al. (2004)             | United Kingdom | 99 (50/49)  | ARM + oxytocin                                      | Water immersion  | Y                  |                   | > 3 cm                    |                                     |
| Cummiskey et al. (1989)          | USA            | 94 (48/46)  | Continuous oxytocin                                 | Pulsatile oxytocin   | Y                  | Y                 | First or second stage     |                                     |
| Curtis et al. (1999)             | USA            | 79 (30/49)  | Oxytocin  | Breast stimulation, delayed oxytocin   | Y                  | Y                 | < 5 cm                    | From 34 weeks                       |
| Dencker et al. (2009)            | Sweden         | 630 (314/316)                                       | Oxytocin within 20 minutes                          | Expectancy three hours   | Y                  |                   | 4–9 cm                    |                                     |
| Grubb et al. (1996)              | USA            | 197 (96/101)  | Oxytocin <sup>fna</sup> ;                           | Out-patient management <sup>fna</sup> ;  |                    | Previous CS       | < 4 cm                    | Latent phase                        |
| Hemminki et al. (1985)           | Finland        | 57 (27/30)  | Oxytocin  | Ambulation   | Y                  | Y                 | First or second stage     |                                     |
| Hinshaw et al. (2008)            | United Kingdom | 412 (208/204)                                       | Oxytocin  | Expectancy eight hours   | Y                  |                   | 3–8 cm                    |                                     |
| Ho et al. (2010)                 | Taiwan         | 231 (113/118)                                       | Oxytocin  | Misoprostol  | Y                  | Y                 | 3–9 cm                    |                                     |
| Jamal and Kalantari (2004)       | Iran           | 200 (100/100)                                       | High dose oxytocin                                  | Low dose oxytocin  | Y                  |                   | > 3 cm                    |                                     |
| Lazor et al. (1993)              | USA            | 467 (224/243) <sup>fnb</sup> ;                      | Oxytocin 15-min interval dose                       | Oxytocin with 40-minute intervals  | Y                  | Y                 | > 3 cm                    |                                     |
| Majoko (2001)                    | Zimbabwe       | 258 (125/133)                                       | High dose oxytocin                                  | Low dose oxytocin  | Y                  |                   | First stage               | From 36 weeks                       |
| Merrill and Zlatnik (1999)       | USA            | 491 (249/242)                                       | High dose oxytocin                                  | Low dose oxytocin  | Y                  | Y                 | > 3 cm                    | From 24 weeks                       |
| Nachum et al. (2010)             | Israel         | 213 (72/71/70) (three arms)                         | Oxytocin/ARM + oxytocin                             | ARM only   | Y                  | Y                 | 2–4 cm                    |                                     |
| Palomäki et al. (2006)           | Finland        | 107 (55/52)   | Propranolol + oxytocin                              | Placebo + oxytocin   | Y                  |                   | First stage               |                                     |
| Read et al. (1981)               | USA            | 14 (6/8)  | Oxytocin  | Ambulation   | Y                  | Y                 | Not specified             |                                     |
| Rouse et al. (1994)              | USA            | 118 (60/58)   | ARM + oxytocin                                      | Oxytocin without ARM   | Y                  |                   | > 4 cm                    | From 36 weeks                       |
| Saunders et al. (1989)           | United Kingdom | 226 (108/118)                                       | Oxytocin  | Placebo  | Y                  |                   | Second stage              | Epidural analgesia                  |
| Sharami et al. (2012)            | Iran           | 118 ('divided randomly')                            | Oxytocin with propranolol                           | Oxytocin with Placebo  | Y                  |                   | 'Active' phase of labour  |                                     |
| Shennan et al. (1995)            | United Kingdom | 93 (46/47)  | Oxytocin  | Placebo  | Y                  |                   | < 7 cm                    | From 36 weeks<br>Epidural analgesia |
| Stein et al. (1990)              | USA            | 65 (30/35)  | Oxytocin  | Nipple stimulation with breast pump <sup>fn</sup> ;‡ + External control group n = 17 | Y                  | Y                 | Unclear                   |                                     |
| Tribe et al. (2012)              | United Kingdom | 502 (250/252)                                       | Continuous infusion of oxytocin                     | Pulsatile infusion of oxytocin   | Y                  | Y                 | First stage               |                                     |

\* If no cervical change after four hours.

† Induction cases excluded.

‡ 18/35 in Nipple stimulation group were switched to oxytocin.

**Table 2**  
Characteristics and inclusion criteria of included systematic reviews.

| Reference            | Total number of participants randomised | Type of intervention               | Comparison group                          | Inclusion criteria   |
|----------------------|---|------------------------------------|---|--|
| Fraser et al. (1998) | 1178 (705/473) (10 trials)              | ARM+early oxytocin                 | Conservative/usual care/amniotomy only    | Randomised and quasi-randomised trials with:<br>Low-risk pregnant women without previous caesarean section with slow progress in the first stage of spontaneous labour at term (37–42 weeks) and a single, cephalic presentation (nulli- and multiparas)                                   |
| Bugg et al. (2013)   | 1338 (eight trials)                     | Oxytocin (low or high dose)        | Placebo or no treatment/delayed treatment | Randomised trials with:<br>Comparison of early amniotomy and oxytocin with conservative management in nulliparous women (nulliparas only, published and unpublished studies), excluded studies where data were not reported by parity  |
| Mori et al. (2011)   | 660 (four trials)                       | High-dose oxytocin                 | Low-dose oxytocin                         | Randomised and quasi-randomised trials with:<br>Comparison of high and low dose oxytocin augmentation for delay in labour (nulli- and multiparas)  |
| Wei et al. (2009)    | 1983 (nine trials)                      | Early oxytocin augmentation        | Conservative approach                     | Randomised trials with:<br>Comparison of early oxytocin augmentation with a more conservative approach and membrane management similar in comparison groups (nulli- and multiparas)  |
| Wei et al. (2012)    | 8033 (14 trials)                        | Early oxytocin and early amniotomy | Expectant management                      | Randomised and quasi-randomised trials with:<br>1. Unselected pregnant women in spontaneous labour; 2. pregnant women in spontaneous labour where there is delay in the first stage (nulli- and multiparas)<br>Excluding: studies where women in both treatment groups underwent amniotomy |

**Table 3**  
Primary and secondary outcomes.

| Outcome  | Number of papers including this outcome (n=33) |      |                        |      |       |      |
|--|--|------|------------------------|------|-------|------|
|  | As a primary outcome                           |      | As a secondary outcome |      | Total |      |
|  | n  | %    | n                      | %    | n     | %    |
| Caesarean section (CS)   | 15   | 45.5 | 2                      | 6.0  | 17    | 51.5 |
| Length of labour (first, second and/or third stages)   | 14   | 42.4 | 7                      | 21.2 | 21    | 63.6 |
| Uterine activity, tachysystole, contractions measured by Montevideo units, hypertonus, uterine hyperstimulation, uterine atony                                       | 13   | 39.4 | 6                      | 18.2 | 19    | 57.6 |
| Mode of birth (forceps/vacuum/SVD), spontaneous vaginal delivery (SVD) within 12/24 hours, vaginal birth after CS  | 9  | 27.3 | 10                     | 30.3 | 19    | 57.6 |
| Umbilical artery pH, acidosis  | 6  | 18.2 | 6                      | 18.2 | 12    | 36.4 |
| Failure to progress, labour augmentation, labour progress, cervical dilatation   | 6  | 18.2 | 1                      | 3.0  | 7     | 21.2 |
| Apgar score, need for resuscitation  | 5  | 15.2 | 17                     | 51.5 | 22    | 66.7 |
| Admission to Special Care Baby Unit, or neonatal complications   | 5  | 15.2 | 13                     | 39.4 | 18    | 54.6 |
| Post partum haemorrhage, blood transfusion   | 5  | 15.2 | 11                     | 33.3 | 16    | 48.5 |
| Effect of oxytocin in various doses, mean oxytocin dose, length of time on oxytocin  | 5  | 15.2 | 10                     | 30.3 | 15    | 45.5 |
| Neonatal/perinatal mortality, or serious perinatal morbidity (e.g. seizures, birth asphyxia defined by trialists, neonatal encephalopathy, disability in childhood)  | 5  | 15.2 | 10                     | 30.3 | 15    | 45.5 |
| Maternal mortality or serious morbidity (e.g. uterine rupture, admission to intensive care unit, septicaemia, placental abruption, chorioamnionitis, antibiotic use) | 5  | 15.2 | 8                      | xx   | 13    | 39.4 |
| Birth weight   | 5  | 15.2 | 5                      | 15.2 | 10    | 30.3 |
| Epidural, analgesia used   | 4  | 12.2 | 11                     | 33.3 | 15    | 45.5 |
| Fetal distress, non-reassuring fetal heart rate, meconium, need for fetal blood sampling   | 3  | 9.1  | 5                      | 15.2 | 8     | 24.3 |
| Episiotomy, vaginal tears  | 3  | 9.1  | 4                      | 12.2 | 7     | 21.2 |
| Maternal satisfaction  | 1  | 3.2  | 4                      | 12.2 | 5     | 15.2 |
| Indication for caesarean section (CS)  | 0  |      | 11                     | 33.3 | 11    | 33.3 |
| Hyperbilirubinaemia/jaundice requiring phototherapy  | 0  |      | 4                      | 12.2 | 4     | 12.2 |
| Discontinued or reduced oxytocin   | 0  |      | 2                      | 6.1  | 2     | 6.1  |
| Mean duration hospital stay  | 0  |      | 2                      | 6.1  | 2     | 6.1  |
| Time from intervention to birth  | 0  |      | 2                      | 6.1  | 2     | 6.1  |
| Placental abruption  | 0  |      | 2                      | 6.1  | 2     | 6.1  |

**Miscellaneous primary outcomes:** Feasibility of full scale RCT, Length of time to rupture of membranes, Number of vaginal exams, Level of presenting part at onset of the second stage, Time necessary to correct labour abnormality after augmentation, Efficacy and safety of a pulsatile regimen.

**Miscellaneous secondary outcomes:** At least one neonatal discharge diagnosis, Neonatal problems, Retained placenta, Anaemia, Birth injuries, Cephalhaematoma, Meconium aspiration, Labour pain, Adverse fetal events, unspecified, Adverse uterine events, 'Other outcomes,' Augmentation, Induction, Amniotomy, Outcomes measured on the Edinburgh Postnatal Depression Scale, Labour Agency Scale, Attitudes Towards the Pregnancy and the Baby Scale, Narcaine given, Treatment side effects, Secondary arrest, Number of vaginal examinations, Use of fetal scalp electrode or uterine pressure catheter, Neonatal vital signs, Maternal and cord plasma levels of propranolol, Neonatal infection, Vaginal birth not achieved within 24 hours, Clinicians' views, Women's perceptions of childbirth one month post partum.

fetal macrosomia and known fetal anomalies. Other exclusion criteria included maternal fever/infection, abnormal bony pelvis, serious maternal disease, prolonged latent phase, high parity and contraindications for trial of labour.

The five reviews included both randomised and quasi-randomised trials, and both published and unpublished studies. Four reviews included studies with both nulliparous and multiparous women. Fraser et al. (1998) included studies of nulliparous

women only (Table 2). Two reviews (Fraser et al., 1998; Wei et al., 2012) included both studies of management of delay in labour and studies of AML (Table 2).

All included trials used oxytocin alone or in combination with artificial rupture of membranes as an intervention. There was a variation of study designs. Some studies compared high or low dose (Bidgood and Steer, 1987a, 1987b; Merrill and Zlatnik, 1999; Majoko, 2001; Jamal and Kalantari, 2004) different increment intervals (Lazor et al., 1993), different measures of (optimal) uterine contractions (Arulkumaran, 1989), continuous versus pulsatile administration (Cummiskey et al., 1989; Tribe et al., 2012), oxytocin versus other active drugs (Ho et al., 2010; Bleich et al., 2011) or in different combinations with placebo (Saunders et al., 1989; Shennan et al., 1995; Palomäki et al., 2006; Sharami et al., 2012) with or without artificial rupture of membranes (Rouse et al., 1994; Blanch et al., 2005; Nachum et al., 2010) or compared to expectancy (Bidgood and Steer, 1987a; Blanch et al., 2005; Hinshaw et al., 2008; Dencker et al., 2009). Not all papers clearly defined the alternative treatment. Some of the studies did use an alternative treatment such as bath (Cluett et al., 2001, 2004), ambulation (Read et al., 1981; Hemminki et al., 1985) and breast or nipple stimulation (Curtis et al., 1999). One study (Lazor et al., 1993) had an intervention also for women with induction of labour and here we only analysed the outcomes of the intervention for women receiving augmentation of labour. One study (Grubb et al., 1996) had an intervention with women in early labour (latent phase) and the intervention was that women with no contractions during four hours were sent home, whilst the other group stayed at hospital and were given oxytocin.

#### Outcome measures

A total of 23 outcome measures that were used in two or more studies or reviews were identified.

#### Primary outcome measures

The most frequently measured primary outcome was caesarean section, occurring in 15 of the 33 publications studied (46%). The length of labour was the next most frequently used ( $n=14$ , 42%), followed by measurements of uterine activity (e.g., hypertonus, uterine hyperstimulation) ( $n=13$ , 39%) and mode of vaginal birth ( $n=9$ , 27%). Umbilical artery pH and the progress of labour were assessed in six studies each (18%). Apgar score, admission to special care baby unit (SCBU), post partum haemorrhage (PPH), the timing and effect of oxytocin, neonatal/perinatal mortality or morbidity, birth weight and maternal mortality or serious morbidity were assessed as primary outcomes in only five (15%) (Table 3).

In relation to women-centred or positive health-focussed outcomes, maternal satisfaction was identified *a priori* by one review (Mori et al., 2011), but was not included as a primary outcome in any individual study included in the review. Spontaneous birth was included only as part of the measurement of mode of birth. No further positive health-focussed outcomes could be identified.

#### Secondary outcome measures

Neonatal outcomes were more commonly assessed as secondary outcomes, with Apgar score/need for resuscitation used in 17 studies (52%) and admission to Special Care Baby Unit (SCBU) in 13 (39%). Post partum haemorrhage/blood transfusion, epidural/analgesia used and the indication for caesarean section were measured in 11 studies (33%). Neonatal/perinatal mortality or morbidity, mode of vaginal birth, and the timing and effect of oxytocin were assessed as secondary outcomes in 10 studies (30%) (Table 3).

Maternal satisfaction was included as a secondary outcome by three papers (Blanch et al., 2005; Cluett et al., 2004; Nachum et al., 2010) and was identified *a priori* by one review (Wei et al., 2009). One study measured women's perceptions of childbirth one month post partum (Bergqvist et al., 2012). The review by Bugg et al. (2013) identified 'woman not satisfied' and 'care-giver not satisfied' as secondary outcomes, but these are negatively-phrased. One study measured rates of breast feeding on discharge (Hemminki et al., 1985). No further women-centred, or positive health-focussed outcomes were identified.

#### Summative view on outcome measures

When all outcomes are combined, the findings demonstrate that more than half of all studies ( $n=22-17$ , 67–52%) assessed caesarean section rates, length of labour, Apgar score, uterine activity, admission to SCBU, and mode of vaginal birth (Table 3). Nearly half measured post partum haemorrhage/blood transfusion, neonatal/perinatal mortality or morbidity, epidural/analgesia used and the timing and effect of oxytocin ( $n=16-15$ , 49–46%). At least one third ( $n=11-13$ , 33–39%) assessed umbilical artery pH, indication for caesarean section and serious maternal morbidity or death. Only five studies (15%) sought women's views on their experiences. A number of miscellaneous outcomes that were included in only one study each was also noted (Table 3).

## Discussion

#### Strengths and limitations

This review has analysed outcome measures used in randomised trials, which will enable clinicians to identify gaps in the published research and what outcomes should be included in future research. Complete retrieval of identified papers was achieved. No quality assessment was conducted as results of trials were not being analysed.

#### Main findings

This systematic review demonstrated that the majority of studies or reviews on using oxytocin to treat delayed progress in labour focus, understandably, on maternal and fetal birth outcomes including caesarean section rates, length of labour, Apgar scores, mode of vaginal birth, uterine activity, admission to SCBU, post partum haemorrhage/blood transfusion, perinatal mortality or morbidity, epidural/analgesia used and the timing and effect of oxytocin. These outcomes are well established and focus mostly on adverse facets. Even the systematic review that did include maternal satisfaction as an outcome, phrased it negatively (Mori et al., 2011). Maternal satisfaction, although very important to include in all maternity care studies, is difficult to ascertain accurately as, even when mothers are not happy with the birth they experienced, they often report 'satisfaction' once a positive outcome has been achieved (Hodnett, 2002). Despite these difficulties, an attempt at measuring maternal satisfaction should be made in all studies of interventions in childbirth.

Devane et al.'s Delphi study of 218 key stakeholders in maternity care (including maternity service users, paediatricians, obstetricians, midwives, general practitioners and policymakers), across 28 countries, outlined a core set of 48 key outcomes that they believed maternity care researchers should assess in future studies evaluating models of maternity care (Devane et al., 2007). The majority of the top 10 outcomes given above were all found in the Delphi study; exceptions were outcomes particular to the type of study (uterine activity, tachysystole, timing and effect of oxytocin in various doses). However, seven arguably appropriate

outcomes of the 48 derived from the Delphi study (birth injury to infant, anal sphincter damage, faecal incontinence, postnatal readmission of mother or neonate, postnatal depression, puerperal psychosis) (Devane et al., 2007) were used in none, or at the most, one, of the studies on using oxytocin to treat delay of progress in labour.

All studies in this review were randomised trials and the reviews were based on, or included, randomised trials. Results of other non-randomised studies regarding possible links between oxytocin use and these outcomes are conflicting, or non-existent. Clavicle damage (Lurie et al., 2011) and brachial plexus injury (Tandon and Tandon, 2005) are, for example, said to be associated with oxytocin use, but the confounding variables of fetal macrosomia and prolonged labour cloud this issue. Although some studies appear to show that oxytocin infusion can lead to anal sphincter damage (Jandér and Lyrenäs, 2001; Nakai et al., 2006) and/or faecal incontinence (Casey et al., 2005), other large cohort studies disagree (Christianson et al., 2003; Jangö et al., 2012). Postnatal readmission of mother or neonate is an outcome studied in relation to care pathways rather than individual intrapartum interventions, so this variable is not present in cohort studies on oxytocin use. No direct association has been shown between oxytocin use and postnatal depression, but postnatal depression is linked with postnatal readmission of the mother (Sword et al., 2011). Given these tentative associations, or lack of evidence, these seven variables would thus be suitable outcomes to consider measuring in future randomised trials of oxytocin use.

Authors of the Delphi study noted that most items in the data set were phrased as adverse outcomes (Devane et al., 2007). This is understandable, as the main purpose of most randomised trials is to test an intervention which sets out, first, to cause no injury and second, to improve birth outcomes for mother and infant. Similarly, almost none of the studies or systematic reviews included in this review refer to women-centred outcomes (e.g., maternal experience of pain, women's views of length of labour) or to positive health-focused outcomes (e.g., intact perineum, maternal self-esteem). Walsh has drawn attention to how women, when discussing their choice of place of birth, did not focus on doctors, provision of epidurals, or facilities for ventouse or caesarean births, so outcomes phrased in this way may have no great meaning for them. Instead, they spoke of the environment (how calm it was, or homely), the social aspect (near home, for visiting, or that family or friends had birthed there), and personal factors (friendliness of staff) (Walsh, 2007). Understanding the importance of such factors may help clinicians to be more positive and mindful in their choice of language when talking with women, concentrating more on environmental, social and personal aspects than on adverse outcomes. Women-centred and positive-focussed outcomes are thus important to measure, in addition to those of interest to clinicians, so that we have results that are pertinent to women.

Phrasing outcomes in a more positive fashion can help to develop a salutogenic focus to health care, which may increase clients' 'sense of coherence' (Lindström and Eriksson, 2006). This assists people, despite experiencing stressful situations, to develop resilience. The need for maternity care researchers to develop tools that measure 'optimality', or the best clinical outcome for the least intervention in childbirth, has been highlighted. An 'optimality index' has been developed and tested in a number of countries (Murphy and Fullerton, 2001; Sheridan and Sandall, 2010) and work is in progress on an international version.

## Conclusion

It is recommended that, in future randomised trials of oxytocin use for slow progress in labour, a number of outcomes from the

core data set developed by Devane et al. (2007) are measured to provide a more complete outcome picture for both mother and infant, in the short and long-term. In addition, including more women-centred and positive health-focussed outcomes may instil a more salutogenic culture in childbirth, with the potential to increase women's resilience and sense of coherence as they progress through childbirth.

## Conflict of interest

None of the authors have any financial, personal, political, intellectual or religious interests that would compete with this work. Two of the authors are also authors of two papers included in the review (Dencker et al. (2009) and Bergqvist et al. (2012)), which were reviewed and included by two of the other reviewers.

## Authors' contributions

All authors have made substantial contributions to all of the following: (1) conception and design of the study, or acquisition of data and analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version submitted.

## Details of ethics approval

As this review was based on data from published literature, ethical approval was not required.

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## References

- Albers, L.L., 1999. The duration of labor in healthy women. *J. Perinatol.* 19, 114–119.
- Arulkumaran, S., Yang, M., Ingemarsson, I., Singh, P., Ratnam, S.S., 1989. Augmentation of labour: does oxytocin titration to achieve preset active contraction area values produce better obstetric outcome? *Asia-Ocean. J. Obstet. Gynaecol.* 15, 333–337.
- Bergqvist, L., Dencker, A., Taft, C., et al., 2012. Women's experiences after early versus postponed oxytocin treatment of slow progress in first childbirth – a randomised controlled trial. *Sex. Reprod. Healthc.* 3, 61–65.
- Bidgood, K., Steer, P., 1987a. A randomized control study of oxytocin augmentation of labour. 1. Obstetric outcome. *Br. J. Obstet. Gynaecol.* 94, 512–517.
- Bidgood, K.A., Steer, P.J., 1987b. A randomized control study of oxytocin augmentation of labour. 2. Uterine activity. *Br. J. Obstet. Gynaecol.* 94, 518–522.
- Blanch, G., Lavender, T., Walkinshaw, S., Alfirevic, Z., 2005. Dysfunctional labour: a randomised trial. *Br. J. Obstet. Gynaecol.* 105, 117–120.
- Bleich, A.T., Villano, K.S., Lo, J.Y., Alexander, J.M., McIntire, D.D., Leveno, K.J., 2011. Oral misoprostol for labor augmentation: a randomized controlled trial. *Obstet. Gynecol.* 118, 1255–1260.
- Bugg, G.J., Siddiqui, F., Thornton, J.G., 2013. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database of Systematic Reviews* 2013, Issue 6. Art. No.: CD007123. <http://dx.doi.org/10.1002/14651858.CD007123.pub3>.

- Bugg, G.J., Stanley, E., Baker, P.N., Taggart, M.J., Johnston, T.A., 2006. Outcomes of labours augmented with oxytocin. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 124, 37–41.
- Casey, B.M., Schaffer, J.I., Bloom, S.L., Heartwell, S.F., McIntire, D.D., Leveno, K.J., 2005. Obstetric antecedents for postpartum pelvic floor dysfunction. *Obstet. Gynecol.* 192, 1655–1662.
- Christianson, L., Bovbjerg, V., McDavitt, E., Hullfish, K., 2003. Risk factors for perineal injury during delivery. *Obstet. Gynecol.* 189, 255–260.
- Clark, S.L., Simpson, K.R., Knox, G.E., Garite, T.J., 2009. Oxytocin: new perspectives on an old drug. *Obstet. Gynecol.* 200 (35 e1–35 e6).
- Cluett, E.R., Pickering, R.M., Brooking, J.I., 2001. An investigation into the feasibility of comparing three management options (augmentation, conservative and water) for nulliparae with dystocia in the first stage of labour. *Midwifery* 17, 35–43.
- Cluett, E.R., Pickering, R.M., Getliffe, K., Saunders, N.J.S.G., 2004. Randomised controlled trial of labouring in water compared with standard of augmentation for management of dystocia in first stage of labour. *Br. Med. J.* 328, 314–318.
- Cohen, G.R., O'Brien, W.F., Lewis, L., Knuppel, R.A., 1987. A prospective randomized study of the aggressive management of early labor. *Am. J. Obstet. Gynecol.* 157, 1174–1177.
- Cummiskey, K.C., Gall, S.A., Dawood, M.Y., 1989. Pulsatile administration of oxytocin for augmentation of labor. *Obstet. Gynecol.* 74, 869–872.
- Curtis, P., Resnick, J.C., Evens, S., Thompson, C.J., 1999. A comparison of breast stimulation and intravenous oxytocin for the augmentation of labor. *Birth* 26, 115–122.
- Day-Stirk, F., Palmer, L., 2003. The RCM virtual institute for birth: promoting normality. *Midwives* 6, 64–65.
- Dencker, A., Berg, M., Bergqvist, L., Ladfors, L., Thorsén, L., Lilja, H., 2009. Early versus delayed oxytocin augmentation in nulliparous women with prolonged labour – a randomised controlled trial. *Br. J. Obstet. Gynaecol.* 116, 530–536.
- Devane, D., Begley, C.M., Clarke, M., Horey, D., O'Boyle, C., 2007. Evaluating maternity care: a core set of outcome measures. *Birth* 34, 164–172.
- Floric, M., Stephansson, O., Nordström, L., 2006. Indications associated with increased caesarean section rates in a Swedish hospital. *Int. J. Gynecol. Obstet.* 92, 181–185.
- Fraser, W., Vendittelli, F., Krauss, I., 1998. Effects of early augmentation of labour with amniotomy and oxytocin in nulliparous women: a meta-analysis. *Br. J. Obstet. Gynaecol.* 105, 189–194.
- Grubb, D.K., Kjos, S.L., Paul, R.H., 1996. Latent labor with an unknown uterine scar. *Obstet. Gynecol.* 88, 351–355.
- Hayes, E.J., Weinstein, L., 2008. Improving patient safety and uniformity of care by a standardized regimen for the use of oxytocin. *Obstet. Gynecol.* 198 (622 e1–622 e7).
- Hemminki, E., Lenck, M., Saarikoski, S., Henriksson, L., 1985. Ambulation versus oxytocin in protracted labour: a pilot study. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 20, 199–208.
- Hinshaw, K., Simpson, S., Cummings, S., Hildreth, A., Thornton, J., 2008. A randomised controlled trial of early versus delayed oxytocin augmentation to treat primary dysfunctional labour in nulliparous women. *Br. J. Obstet. Gynaecol.* 115, 1289–1296.
- Ho, M., Cheng, S.Y., Li, T.C., 2010. Titrated oral misoprostol solution compared with intravenous oxytocin for labor augmentation: a randomized controlled trial. *Obstet. Gynecol.* 116, 612–618.
- Hodnett, E.D., 2002. Pain and women's satisfaction with the experience of childbirth: a systematic review. *Am. J. Obstet. Gynecol.* 186, S 160–S 172.
- Jamal, A., Kalantari, R., 2004. High and low dose oxytocin in augmentation of labor. *Int. J. Gynecol. Obstet.* 87, 6–8.
- Jandér, C., Lyrenäs, S., 2001. Third and fourth degree perineal tears. *Acta Obstet. Gynecol. Scand.* 80, 229–234.
- Jangö, H., Langhoff-Roos, J., Rosthøj, S., Sakse, A., 2012. Risk factors of recurrent anal sphincter ruptures: a population-based cohort study. *Br. J. Obstet. Gynaecol.* 119, 1640–1647.
- Lazor, L.Z., Philipson, E.H., Ingardia, C.J., Kobetsch, E.S., Curry, S.L., 1993. A randomized comparison of 15- and 40-minute dosing protocols for labor augmentation and induction. *Obstet. Gynecol.* 82, 1009–1012.
- Liberati, A., Altman, D.G., Tetzlaff, J., et al., 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med.* 6, 1–28, e1000100.
- Lindström, B., Eriksson, M., 2006. Contextualizing salutogenesis and antonovsky in public health development. *Health Promot. Int.* 21, 238–244.
- Lurie, S., Wand, S., Golan, A., Sadan, O., 2011. Risk factors for fractured clavicle in the newborn. *J. Obstet. Gynaecol. Res.* 37, 1572–1574.
- Majoko, F., 2001. Effectiveness and safety of high dose oxytocin for augmentation of labour in nulliparous women. *Cent. Afr. J. Med.* 47, 247–250.
- Merrill, D.C., Zlatnik, F.J., 1999. Randomized, double-masked comparison of oxytocin dosage in induction and augmentation of labor. *Obstet. Gynecol.* 94, 455–463.
- Mori, R., Tokumasu, H., Pledge, D., Kenyon, S., 2011. High dose versus low dose oxytocin for augmentation of delayed labour. *Cochrane Database of Systematic Reviews*. October 5;(10)(10):CD007201.
- Murphy, P.A., Fullerton, J.T., 2001. Measuring outcomes of midwifery care: development of an instrument to assess optimality. *J. Midwifery Womens Health* 46, 274–281.
- Nachum, Z., Garmi, G., Kadan, Y., Noah, Z., Shalev, E., Salim, R., 2010. Comparison between amniotomy, oxytocin or both for augmentation of labor in prolonged latent phase: a randomized controlled trial. *Reprod. Biol. Endocrinol.* 8, 136–143.
- Nakai, A., Yoshida, A., Yamaguchi, S., et al., 2006. Incidence and risk factors for severe perineal laceration after vaginal delivery in Japanese patients. *Arch. Gynecol. Obstet.* 274, 222–226.
- Neal, J.L., Lowe, N.K., Ahijevych, K.L., Patrick, T.E., Cabbage, L.A., Corwin, E.J., 2010. 'Active labor' duration and dilation rates among low-risk, nulliparous women with spontaneous labor onset: a systematic review. *J. Midwifery Womens Health* 55, 308–318.
- Oscarsson, M.E., Amer-Wählin, I., Källén, K., 2006. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet. Gynecol. Scand.* 85, 1094–1098.
- Palomäki, O., Uotila, J., Tammela, O., et al., 2006. A double blind, randomized trial on augmentation of labour with a combination of intravenous propranolol and oxytocin versus oxytocin only. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 125, 44–49.
- Read, J., Miller, F., Paul, R., 1981. Randomized trial of ambulation versus oxytocin for labor enhancement: a preliminary report. *Obstet. Gynecol.* 139, 669–672.
- Rooks, J.P., 2009. Oxytocin as a 'high alert medication': a multilayered challenge to the status quo. *Birth* 36, 345–348.
- Rouse, D.J., McCullough, C., Wren, A.L., Owen, J., Hauth, J.C., 1994. Active-phase labor arrest: a randomized trial of chorioamniotic management. *Obstet. Gynecol.* 83, 937–940.
- Saunders, N., Spiby, H., Gilbert, L., et al., 1989. Oxytocin infusion during second stage of labour in primiparous women using epidural analgesia: a randomised double blind placebo controlled trial. *Br. Med. J.* 299, 1423–1426.
- Sharami, S., Milani, F., Tofighi, M., Salamt, F., Dalil Heirati, S.F., 2012. Effect of oxytocin plus propranolol on the success of labor augmentation. *J. Guilan Univ. Med. Sci.* 21, 57–64 (abstract).
- Shennan, A., Smith, R., Browne, D., Edmonds, D., Morgan, B., 1995. The elective use of oxytocin infusion during labour in nulliparous women using epidural analgesia: a randomised double-blind placebo-controlled trial. *Int. J. Obstet. Anesth.* 4, 78–81.
- Sheridan, M., Sandall, J., 2010. Measuring the best outcome for the least intervention: can the optimality index-US be applied in the UK? *Midwifery* 26, e9–e15.
- Smith, V., Daly, D., Lundgren, I., Eri, T., Benstoem, C., Devane, D., 2014. Salutogenically focused outcomes in systematic reviews of intrapartum interventions: a systematic review of systematic reviews. *Midwifery* 30, e151–e156.
- Stein, J., Bardeguéz, A., Verma, U., Tegani, N., 1990. Nipple stimulation for labor augmentation. *J. Reprod. Med.* 35, 710–714.
- Sword, W., Kurtz Landy, C., Thabane, L., et al., 2011. Is mode of delivery associated with postpartum depression at 6 weeks: a prospective cohort study. *Br. J. Obstet. Gynaecol.* 118, 966–977.
- Tandon, S., Tandon, V., 2005. Primiparity: a risk factor for brachial plexus injury in the presence of shoulder dystocia? *J. Obstet. Gynecol.* 25, 465–468.
- Tribe, R.M., Crawshaw, S.E., Seed, P., Shennan, A.H., Baker, P.N., 2012. Pulsatile versus continuous administration of oxytocin for induction and augmentation of labor: two randomized controlled trials. *Am. J. Obstet. Gynecol.* 206, e1–e8.
- Vahratian, A., Troendle, J.F., Siega-Riz, A.M., Zhang, J., 2006. Methodological challenges in studying labour progression in contemporary practice. *Paediatr. Perinat. Epidemiol.* 20, 72–78.
- Waldenström, U., Hildingsson, I., Rubertsson, C., Rådestad, I., 2004. A negative birth experience: prevalence and risk factors in a national sample. *Birth* 31, 17–27.
- Walsh, D., 2007. Childbirth beyond models. In: Walsh, D. (Ed.), *Improving Maternity Services. Small is Beautiful: Lessons from a Birth Centre*. Radcliffe Publishing Ltd., UK, pp. 84–101.
- Wei, S.Q., Luo, Z.C., Qi, H.P., Xu, H., Fraser, W.D., 2010. High-dose vs low-dose oxytocin for labor augmentation: a systematic review. *Am. J. Obstet. Gynecol.* 203, 296–304.
- Wei, S., Wo, B.L., Qi, H.P., et al., 2012. Early amniotomy and early oxytocin for prevention of, or therapy for, delay in first stage spontaneous labour compared with routine care. *Cochrane Database of Systematic Reviews*. 12;9:CD006794.
- Wei, S.Q., Luo, Z.C., Xu, H., Fraser, W.D., 2009. The effect of early oxytocin augmentation in labor: a meta-analysis. *Obstet. Gynecol.* 114, 641–649.
- Xenakis, E.M.J., Langer, O., Piper, J.M., Conway, D., Berkus, M.D., 1995. Low-dose versus high-dose oxytocin augmentation of labor – a randomized trial. *Obstet. Gynecol.* 173, 1874–1878.