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**ORIGINAL ARTICLE** ***Psychology and counselling***

# Factors influencing women's preferences for subsequent management in the event of incomplete evacuation of the uterus after misoprostol treatment for miscarriage

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**STUDY QUESTION:** What affects women's treatment preferences in the management of an incomplete evacuation of the uterus after misoprostol treatment for a first-trimester miscarriage?

**SUMMARY ANSWER:** Women's treatment preferences in the management of an incomplete evacuation of the uterus after misoprostol treatment for miscarriage are most strongly influenced by 'the risk of a reduced fertility' followed by 'the probability of success'.

**WHAT IS KNOWN ALREADY:** Available treatment options in miscarriage are surgical, medical or expectant management. Treatment with misoprostol leads to an incomplete evacuation of the uterus and additional surgical treatment in 20–50% of women. To our knowledge, women's preferences for subsequent treatment of an incomplete evacuation of the uterus after misoprostol treatment for miscarriage have not been studied yet.

**STUDY DESIGN, SIZE, DURATION:** Between April 2014 and January 2015, we conducted a prospective nationwide multicentre discrete-choice experiment (DCE). DCEs have become the most frequently applied approach for studying patient preferences in health care. In our DCE, which considerers five attributes, a target sample size was calculated including 20 patients per attribute for the main analysis. We intended to include 25% more patients, i.e. a total of 125 thus enabling us to assess heterogeneity of treatment choices.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** All women visiting the outpatient clinic with first-trimester miscarriage or incomplete miscarriage were invited to participate in the study. Women under 18 years of age, women who were unable to understand the Dutch questionnaire or women who already had received a treatment for the current miscarriage were excluded. Women's preferences were assessed using a DCE. A literature review, expert opinions and interviews with women from the general population were used to define relevant treatment characteristics. Five attributes were selected: (i) certainty about the duration of convalescence; (ii) number of days of bleeding after treatment; (iii) probability of success (empty uterus after treatment); (iv) risk of reduced fertility and (v) risk of complications requiring more time or readmission to hospital. Fourteen scenarios using these attributes were selected in the DCE. Each of these scenarios presented two treatment options, while treatment characteristics varied between the 14 scenarios. For each scenario, respondents were asked to choose the preferred treatment option. The importance of each attribute was analysed, and preference heterogeneity was investigated through latent-class analysis.

**MAIN RESULTS AND THE ROLE OF CHANCE:** One hundred and eighty-six women were included of whom 128 completed the DCE (69% response rate). The two attributes with the greatest effect on their preference were, probability of success and risk of reduced fertility. The latent-class analysis revealed two subgroups of patients with different preference patterns. Forty per cent of women were more influenced by treatment success and 59% were more influenced by risk.

**LIMITATIONS, REASONS FOR CAUTION:** Most women were highly educated and were of Dutch origin, which limits the generalizability of our findings. Women with lower education levels, other cultural backgrounds and/or different previous experiences may differ from our findings.

**WIDER IMPLICATIONS OF THE FINDINGS:** Patients preferences should be addressed when counselling patients with an incomplete miscarriage after misoprostol treatment.

**STUDY FUNDING/COMPETING INTEREST(S):** This study was embedded in the MisoREST trial, and funded by ZonMw, a Dutch organization for Health Research and Development, project number 80-82310-97-12066. There were no conflicts of interests.

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**Key words:** counselling / abortion / ethics / pregnancy termination

# Introduction

First-trimester miscarriage occurs in 10–15% of pregnant women and results in 8000 to 27 000 miscarriages in the Netherlands each year (Dutch Hospital Data, 2009). In the past, women who had a miscarriage were either managed expectantly or were offered surgical treatment (i.e. curettage) (Wieringa-de Waard *et al.*, 2002, 2004). There is no doubt that curettage is an effective treatment for women with a miscarriage, but it bears the risk of uterine perforation and the formation of intra-uterine adhesions, in particular in women with a previous curettage (Schenker and Margalioth, 1982; Hooker *et al.*, 2013).

More recently, medical treatment with misoprostol has been introduced as a cost-effective non-surgical alternative (Ngai *et al.*, 2001; You and Chung, 2005; Elati and Weeks, 2009; Niinimäki *et al.*, 2009; Rausch *et al.*, 2012; Tang *et al.*, 2013). Treatment with misoprostol leads to an incomplete evacuation of the uterus in 20–50% of treated women (Bagratee *et al.*, 2004; Graziosi *et al.*, 2004; Zhang *et al.*, 2005; Trinder *et al.*, 2006; Ankum, 2008; Prasad *et al.*, 2009). Although most women with an incomplete evacuation are relatively asymptomatic, this ultrasound finding often leads to additional surgical intervention (Creinin *et al.*, 2004; Davis *et al.*, 2004).

We recently compared the cost and effects of expectant management versus surgical treatment in women with incomplete miscarriages after misoprostol treatment (Lemmers *et al.*, 2016). In our trial, women were randomly allocated to either expectant management or curettage. Women who refused randomization were asked to participate in a cohort study and received the treatment of their preference. Strikingly, of 256 participating women only 59 (23%) accepted randomization which illustrates the presence of strong treatment preferences in this clinical situation.

In recent years, discrete-choice experiments (DCEs) have become the acknowledges approach for studying patient preferences in health care (Reed Johnson *et al.*, 2013). The method involves asking individuals to indicate their preference in hypothetical alternative scenarios by offering a series of choice sets from which they are to choose their preferred alternatives. The choice sets contain several treatment characteristics of interest, so called attributes (Streets *et al.*, 2005; Mangham *et al.*, 2008).

Our aim in the present study was to analyze women's treatment preferences in case of an incomplete evacuation of the uterus after misoprostol treatment for miscarriage, by means of a DCE.

# Materials and Methods

## Study design

All women visiting the outpatient clinic with first-trimester miscarriage were invited to participate in the DCE. Participants received a questionnaire that included 14 scenarios. Each of the scenarios comprised two treatment options of which treatment characteristics varied between the 14 scenarios. For each scenario, respondents were asked to choose the preferred treatment option (Table I). The generated treatment options were fictional. These included features (i.e. levels) matching with both expectant management and surgical treatment.

The DCE design of this study was based on the widely acknowledged recommendations of the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) for good research practices for conjoint analysis task force (Bridges *et al.*, 2011).

### *Identifying attributes and assigning levels*

In defining the attributes in our DCE, we used a literature review, expert opinions, and interviews with women from the general population. The literature review was used to identify attributes which had already been used in previous studies on the management of first-trimester miscarriage and their consequences in general (Chipchase and James, 1997; Ryan and Hughes, 1997; Westendorp *et al.*, 1998; Demetroulis *et al.*, 2001; Wieringa-de Waard *et al.*, 2004; Petrou and McIntosh, 2009; Hooker *et al.*, 2013). These were discussed in a focus group of experts specialized in preference studies. To identify attributes of interest within the general population, 14 women without a medical background were interviewed.

This resulted in a total of 26 possible attributes of interest (Table II). No studies assessed the maximum amount of attributes before the choice task gets too complicated, although there is an assumption that four to six

**Table I Example of a choice set as included in the DCE.**

| Scenario 1 | Fictional treatment A | Fictional treatment B |
|---|---|---|
| Certainty about duration of course | Uncertain | Certain |
| Number of days of bleeding after treatment | Less than 1 day | Less than 1 day |
| Probability of success | 85% (85 out of 100) | 98% (98 out of 100) |
| Chance of reduced fertility | Not increased | Not increased |
| Chance of complications requiring more time or readmission to hospital | Very unlikely (5 out of 100) | Quite unlikely (10 out of 100) |
| For scenario 1, which treatment do you prefer *(tick one box only)*? | Prefer treatment A | Prefer treatment B |
| | ☐ | ☐ |

DCE, discrete-choice experiment.

attributes is ideal (Ryan and Gerard, 2003). Some attributes that were quite similar were merged together. Attributes that did not differ between expectant management and surgical management were excluded. Attributes coverings the subject of 'willingness to pay' were also excluded, since the Dutch insurance system covers the treatment of miscarriage.

Five attributes were selected: (i) certainty about the duration of convalescence; (ii) number of days of bleeding after treatment; (iii) probability of success (empty uterus after treatment); (iv) risk of reduced fertility and (v) risk of complications requiring more time or readmission to hospital. The selected attributes, therefore, covered the areas of 'effectiveness' 'burden' and 'safety'.

The levels assigned to these attributes were based on literature data. Levels which differed the most between expectant management and surgical treatment were selected (Tables III and IV).

### *Questionnaire design*

The five attributes and their levels generated a total of 72 ($2^3 \times 3^2$) possible scenarios. Obviously, this number is too large for participants to stay focused. The solution to this problem is to use only a fraction of the possible scenarios. Therefore, a fractional factorial design was used to draw an independent sample of scenarios from the full factorial set. We used Ngene design software to draw a most efficient design (version 1.1.1 Choicemetrics Pty Ltd, Sydney, NSW, Australia). Thirteen scenarios were selected, thus meeting the main criteria for an efficient DCE design: level balance; minimal overlap; and near orthogonality (Huber and Zwerina, 1996; Ryan and Hughes, 1997). We included a check for internal consistency by adding a dominant test (Table V). In this specific scenario treatment A is set to be optimal, i.e. all levels are equal or better compared to treatment B. Whenever a participant preferred treatment B, this implied that she failed to understand the questionnaire. Therefore, the results of this participant were not valid and could not be used for analysis.

Thus, in total, 14 scenarios were included in the questionnaire, 13 from the fractional factorial design and the internal consistency check. Additional questions about baseline characteristics of the participants and a fictive case scenario (described below) were added.

## Pilot testing

Before starting our actual DCE, we performed a pilot study in a clinical setting among 30 patients, in order to identify any inconsistencies in the questionnaire (Carlsson and Martinsson, 2003; Lancsar and Louviere, 2008). The dominant test was filled in correctly by 29 of 30 women. Analysis was performed by a multinomial logistic (MNL) regression model. The MNL model converts the observed choice frequencies into utility (value) true the logistic function. The utility associated with every attribute level can be estimated. Analysis of these 29 respondents showed consequent choices between the various attribute levels. This confirmed the direction of the effect of the attributes to be as expected. It also showed that all attributes had a significant effect on the choice option. Therefore, the DCE pilot version is considered valid in terms of basic MNL analysis.

## Sample size

A target sample size with the use of five attributes was calculated by using a rule of thumb of 20 patients per attribute for the main analysis. We intended to include 25% patients more, i.e. a total of 125 thus enabling us to assess heterogeneity across choices.

## Participants

All women visiting the outpatient clinic with first-trimester miscarriage or incomplete miscarriage were invited to participate in the study. Women under 18 years of age, women who were unable to understand the Dutch questionnaire or women who already received any type of treatment for the current miscarriage were excluded. All included women received a questionnaire with a stamped addressed envelope before treatment of the current miscarriage was started. If the questionnaire had not been returned within two weeks, a reminder was sent.

The questionnaire started with a fictive case scenario of a patient who would be suitable to be included in the MisoREST trial. We asked each woman to imagine herself in the following situation: 'You visit the outpatient clinic where a miscarriage is diagnosed by ultrasound, the heart of the baby is not beating or there is an empty gestational sac. After this diagnosis you received medical treatment to induce the miscarriage. After this treatment you visit the outpatient clinic again. Unfortunately, with ultrasound the doctor confirmed the uterus was not completely empty. The miscarriage is not yet complete.' After reading the case, all participants had to choose between either fictional treatment A or B for each of the 14 scenarios presented to them.

Finally, the participants were asked some demographic baseline characteristics, i.e. obstetric history, past miscarriage(s) and its treatment, gestational age at diagnosis of the miscarriage and preference of treatment for the current miscarriage.

## Statistical methods

We estimated the importance that patients placed on each attribute level using a main-effects (no interactions) multinomial logit model as recently described (Hazlewood *et al.*, 2016). The importance of each attribute was inferred from patients' responses across the choice tasks. The model assumed the probability of a participant choosing a given treatment within the set of choices to be related to an overall value (utility) of each treatment plus a random error. The overall value of the treatment was defined as the sum of the importance scores for the attribute levels which define the treatment.

**Table II Possible attributes of interest, split into founded by literature, expert opinion or interviews.**[a]

Literature
- Number of days of bleeding after treatment □
- Probability of success □ ●
- Chance of complications requiring more time or readmission to hospital □ ●
- Complications following treatment □ ●
- Side-effects during and immediately after treatment
- Level of pain experienced during treatment □
- Number of days of analgesia use
- Days of pelvic pain after treatment
- Time spent in hospital receiving treatment
- Time taken to return to normal activities after treatment □ ●
- Time off work (days)
- Travel costs
- Treatment costs
- Duration of treatment
- Waiting time □
- Number of outpatient visits □

Expert opinion
- Certainty about duration of course ●
- Change of reduced fertility ●
- Requiring general anaesthesia ●
- Willingness to pay

Interviews
- Emotional impact of treatment
- Opinions of family and friends
- Medication necessary for treatment
- Negative experiences in the past

● Possible attribute was also mentioned during interviews with the general population.
□ Possible attribute was also mentioned during meetings in the focus group.
[a]Process started with a literature review. Only additional found attributes in focus group and during interviews with women from the general population are shown above.

**Table III Attribute and levels used in the DCE design.**

| Attribute | Levels |
|---|---|
| Certainty about duration of course | Certain<br>Uncertain |
| Number of days of bleeding after treatment | Less than 1 day<br>Between 1 and 7 days<br>Between 7 and 14 days |
| Probability of success | 85% (85 out of 100)<br>98% (98 out of 100) |
| Chance of reduced fertility | Increased<br>Not increased |
| Chance of complications requiring more time or readmission to hospital | Very unlikely (5 out of 100)<br>Quite unlikely (10 out of 100)<br>Unlikely (15 out of 100) |

The attributes were primarily included as categorical variables, then as continuous variables after confirming a linear relationship through visual inspection and by comparing the Akaike information criterion (AIC) between models.

A statistically significant coefficient indicated that respondents considered that particular attribute as important. Absolute values of the dependent variable and coefficients, however, were considered to have no direct interpretation (Louviere *et al.*, 2000). We also determined the increase in the chance of a major symptom improvement required for patients to accept a treatment with an undesirable attribute [marginal rate of substitution (MRS)]. The MRS was calculated by dividing the difference in the importance scores between the highest and lowest attribute levels by the importance of a major symptom improvement, modelled as a continuous variable. The median and 95% confidence Intervals (CIs) of the MRS were estimated through Monte Carlo sampling (Berg, 2004).

Preference heterogeneity was investigated through latent-class analysis (LCA). With LCA one can study whether groups of patients have comparable patterns of preference allowing the estimation that each patient belongs to a certain class. We fitted latent-class solutions with two and three classes, comparing measures of model fit (adjusted Bayesian information criterion and consistent AIC) and patterns of importance scores between models and to the overall multinomial logit model. Patients were assigned to the latent class for which they had the highest probability. We determined the association between selected patient characteristics and latent-class membership using univariate and multivariable logistic regression models. Multivariable models were considered exploratory and were limited to a maximum of seven variables to avoid overfitting. Age and experience with curettage were included a priori in view of their expected preference effect to these attributes on choice-making. Other variables were included based on the results of univariate statistics (all variables had *P*-values < 0.15). All analyses were performed using SPSS 22 (IBM) and R (version 3.1.2; http://www.r-project.org).

## Ethical approval

Ethical approval for this study was proposed from the Medical Ethical Committee of the Academic Medical Centre of Amsterdam (METC project number W14_152). In all seven participating hospitals, approval was acquired from the boards of management.

# Results

The study was performed between April 2014 and January 2015 in seven hospitals in the Netherlands. During the study period, a total of 185 women were eligible and received the questionnaire of which 128 were returned (response rate 69%).

## General characteristics

The baseline characteristics of the women are presented in Table VI. The mean age was 33 years and the mean gestational age was 8.9 weeks. Most women were Western-European (95.2%) and were highly educated (96.8%). A total of 44 women (35%) had experienced at least one miscarriage before.

## Attributes defining the choice for treatment

All five attributes contributed significantly to patients' stated choice ($P < 0.001$) (Table VII). The coefficients indicate the importance of the attribute levels and were logical in their direction.

In the questionnaire, a choice set was added with a dominant test. A 125 of 128 women answered the dominant test as expected. Results were similar when excluding the women who failed the dominant test. Women expressed a clear preference for decreased levels of all five attributes.

**Table IV Pretrial scenarios for expectant and surgical management of miscarriage based on trial attributes and levels.**

| Attribute | Expectant management | Surgical management |
|---|---|---|
| Certainty about duration of course | Uncertain | Certain |
| Number of days of bleeding after treatment | Between 7 and 14 days | Between 1 and 7 days |
| Probability of success | 85% (85 out of 100) | 98% (98 out of 100) |
| Chance of reduced fertility | Not increased | Increased |
| Chance of complications requiring more time or readmission to hospital | Very unlikely (5 out of 100)[a] | Very unlikely (5 out of 100)[a] |

[a]Assumption; not enough literature was found.

**Table V Dominant test included in DCE design for internal validity.**

| Scenario 8 | Fictional treatment A | Fictional treatment B |
|---|---|---|
| Certainty about duration of course | Certain | Uncertain |
| Number of days of bleeding after treatment | Less than 1 day | Between 7 and 14 days |
| Probability of success | 98% (98 out of 100) | 98% (98 out of 100) |
| Change of reduced fertility | Not increased | Increased |
| Change of complications requiring more time or readmission to hospital | Very unlikely (5 out of 100) | Very unlikely (5 out of 100) |
| For scenario 8, which treatment do you prefer *(tick one box only)*? | Prefer treatment A ☐ | Prefer treatment B ☐ |

The negative coefficient of certainty about duration of convalescence (−0.64) indicates that women prefer to know for how long the miscarriage will pursue. The negative coefficient of probability of success (−2.0) indicates that women prefer the treatment with the highest chance of success. The positive coefficient of risk of reduced fertility (2.25) indicates future fertility to be of great importance.

The higher a coefficient, the more important an attribute level was compared to its worst level. In our DCE, two attributes had the strongest coefficient value; probability of success and risk of reduced fertility.

### Preference heterogeneity (latent-class analysis)

The latent-class analysis revealed two subgroups of patients with different preference patterns. In the two-group solution, 41% of patients formed a subgroup that was more success-driven. The other subgroup, 59% of patients, were risk averse (Tables VIIIa–c and IX). The success-driven women considered the probability of treatment success to be more important in comparison to those women who were risk averse (3.6 [3.3–3.9] versus 2.6 [2.3–2.9]). The risk averse women attached more value to a reduced risk of fertility loss (4.5 [3.7–5.3] versus 2.9 [2.0–3.9]). Table X presents the patient characteristics of these subgroups.

## Discussion

### Principal findings

We performed a preference study among 128 women with a recently diagnosed miscarriage.

All five selected attributes played a significant role in women's preferences for additional treatment in case of an incomplete evacuation of the uterus after misoprostol treatment for miscarriage. Two of five attributes were scored the highest: the probability of success and the risk of reduced fertility. These are contradictive since curettage generates the highest success rate but also increases the risk of impaired fertility by the formation of intra-uterine adhesions.

### Strengths and limitations

This study has certain *strengths* and *limitations*. DCEs are increasingly being used in health studies (Ryan and Gerard, 2003). To ensure that the design of our DCE study was correct, we used the checklist of the report *Conjoint Analysis Applications in Health – A Checklist: A Report of the ISPOR Good Research Practices for Conjoint Analysis Task Force* (Reed Johnson *et al.*, 2013). All conditions for conducting a proper DCE study were met in our study. A 97.6% of women answered the dominant test as expected. We, therefore, assume that the majority of women could understand the choice experiment adequately.

The study design used offers a useful empirical approach to overcome generalizability limitations of a randomized controlled trial caused by selective participation resulting from treatment preferences (Wieringa-de Waard *et al.*, 2004).

This study has also limitations. We only included women who were able to read the Dutch questionnaire and understand the trade-off. Most women were highly educated and were from Dutch origin, which limits the generalizability of our findings. Possibly, preferences of women with different education levels, different cultural backgrounds and different previous experiences may differ from our findings. We also did not ask the participants to rank the attributes

**Table VI Patient characteristics of responders at inclusion.**[a]

| Characteristic | Mean (range) |
|---|---|
| Mean age in years | 33 (24–43) |
| Gestational age in weeks | 8.9 (5–12) |
| **Characteristic** | ***N* (%)** |
| Parity | |
| 0 | 61 (48.8) |
| 1 | 46 (36.8) |
| >1 | 18 (14.4) |
| Previous miscarriage treatment* | |
| No miscarriage | 81 (63.8) |
| Expectant management | 22 (17.3) |
| Expectant management followed by curettage | 3 (2.4) |
| Curettage | 6 (4.7) |
| Medical treatment | 10 (7.9) |
| Medical treatment followed by curettage | 5 (3.9) |
| Preferred treatment at inclusion | |
| Expectant management | 43 (34.4) |
| Curettage | 24 (19.2) |
| Medical treatment | 54 (43.2) |
| No preference | 4 (3.2) |
| Native country | |
| Western-Europe | 119 (95.2) |
| Other | 6 (4.8) |
| Level of education | |
| Primary education | 1 (0.8) |
| Secondary education | 2 (1.6) |
| Tertiary education | 121 (96.8) |

*$N = 127$, two responders had two previous miscarriages with different treatments in the past.
[a]Responders, $N = 125$.

**Table VII Multinomial regression results: relative importance per attribute level.**

| Attribute | Level | Coefficient (95% CI) |
|---|---|---|
| Certainty about duration of course | Uncertain | −0.64 (−0.89; −0.39) |
| | Certain | 0 |
| Number of days of bleeding after treatment | Less than 1 day | 0.33 (0.21; 0.45) |
| | Between 1 and 7 days | 0.30 (0.14; 0.46) |
| | Between 7 and 14 days | 0 |
| Probability of success | 85% (85 out of 100) | −2.0 (−2.2; −1.8) |
| | 98% (98 out of 100) | 0 |
| Chance of reduced fertility | Not increased | 2.25 (2.01; 2.40) |
| | Increased | 0 |
| Chance of complications requiring more time or readmission to hospital | Very unlikely (5 out of 100) | 0.88 (0.78; 0.98) |
| | Quite unlikely (10 out of 100) | 0.66 (0.52; 0.81) |
| | Unlikely (15 out of 100) | 0 |

CI, confidence interval.

**Table VIIIa Overall analysis—assuming choices were success-driven.**

| Attribute | Level | Assuming choices were success-driven (100%) |
|---|---|---|
| Probability of success | 85% | −2.96 (−3.15 to −2.76) |
| | 98% | 2.96 (2.76 to 3.15) |
| Chance of reduced fertility | Not increased | 3.32 (2.54 to 4.09) |
| | Increased | −3.32 (−4.09 to −2.54) |
| Certainty about duration of course | Certain | 0.64 (0.4 to 0.9) |
| | Uncertain | −0.64 (−0.9 to −0.4) |
| Number of days of bleeding after treatment | Less than 1 day | 0.33 (0.21 to 0.45) |
| | Between 1 and 7 days | 0.30 (0.14 to 0.46) |
| | Between 7 and 14 days | Reference |
| Chance of complications requiring more time or readmission to hospital | Linear (5–15%) | 0.17 (0.15 to 0.20) |
| Intercept | −1.01 (−1.47 to −0.54) | |
| Log-likelihood | −1797 | |
| cAIC | 3482 | |
| aBIC | 3398 | |

cAIC, consistent Akaike information criterion; aBIC, adjusted Bayesian information criterion.
Data represent means (95% confidence intervals).

from most important to least important, i.e. we did not formally check the convergent validity. There has been no other DCE in this field and therefore we could not determine the external validity of the present study. An intrinsic problem with all surveys is that we cannot ask individuals about everything. In practice, not all possible scenarios could be included in the questionnaire, because of diminishing focus of participants whenever questionnaires are too long (Carlsson and Martinsson, 2003). There is still much debate in health care research as to the appropriate number of scenarios a respondent can complete, but it is good practice to include 8 to 16 conjoint analysis tasks (Bridges *et al.*, 2011).

Finally, the greatest limitation of our study is the scenario itself. One might argue that only patients who actually have experienced a certain disease or treatment are fully able to understand its burdens an can make a balanced choice between advantages and disadvantages of a particular treatment (Graziosi *et al.*, 2006). The case of the incomplete evacuation of the uterus after misoprostol treatment requires some imagination of the woman, which narrows the window of applicability. We attempted to overcome this by including women who experienced a miscarriage in reality, so the emotional state of mind would be similar to those of women who experienced an incomplete miscarriage.

**Table VIIIb Two latent-class analysis.**

| Attribute | Level | Success-driven 41% of women | Risk averse 59% of women |
|---|---|---|---|
| Probability of success | 85% | −3.6 (−3.9 to −3.3) | −2.6 (−2.9 to −2.3) |
| | 98% | 3.6 (3.3 to 3.9) | 2.6 (2.3 to 2.9) |
| Chance of reduced fertility | Not increased | 2.9 (2.0 to 3.9) | 4.5 (3.7 to 5.3) |
| | Increased | −2.9 (−3.9 to −2.0) | −4.5 (−5.3 to −3.7) |
| Certainty about duration of course | Certain | 0.58 (0.32 to 0.84) | 0.72 (0.56 to 0.89) |
| | Uncertain | −0.58 (−0.84 to 0.32) | −0.72 (−0.89 to −0.56) |
| Number of days of bleeding after treatment | Less than 1 day | 0.05 (−0.17 to 0.27) | 0.62 (0.31 to 0.93) |
| | Between 1 and 7 days | 0.04 (−0.15 to 0.23) | 0.53 (0.24 to 0.82) |
| | Between 7 and 14 days | Reference | Reference |
| Chance of complications requiring more time or readmission to hospital | Linear (5–15%) | 0.12 (0.09 to 0.15) | 0.22 (0.18 to 0.26) |
| Log-likelihood | −1642 | | |
| cAIC | 3206 | | |
| aBIC | 3197 | | |

Data represent means (95% confidence intervals).

**Table VIIIc Three latent-class analysis.**

| Attribute | Level | Success-driven 41% of women | No fertility loss 43% of women | Least complications 13% of women |
|---|---|---|---|---|
| Probability of success | 85% | −3.6 (−4.0 to −3.3) | −2.7 (3.1 to −2.4) | 1.5 (−2.1 to 0.94) |
| | 98% | 3.6 (3.3 to 4.0) | 2.7 (2.4 to 3.1) | 1.5 (0.94 to 2.1) |
| Chance of reduced fertility | Not increased | 2.8 (1.7 to 3.9) | 5.5 (4.7 to 6.3) | 4.1 (2.6 to 5.6) |
| | Increased | −2.8 (−3.9 to −1.7) | −5.5 (−6.3 to −4.7) | −4.1 (−5.6 to −2.6) |
| Certainty about duration of course | Certain | 0.59 (0.32 to 0.86) | 0.62 (0.44 to 0.80) | 1.34 (0.96 to 1.72) |
| | Uncertain | −0.59 (−0.86 to −0.32) | −0.62 (−0.8 to −0.44) | −1.34 (−1.72 to −0.96) |
| Number of days of bleeding after treatment | Less than 1 day | 0.05 (−0.17 to 0.27) | 0.62 (0.31 to 0.93) | 1.82 (1.33 to 2.31) |
| | Between 1 and 7 days | 0.04 (−0.15 to 0.23) | 0.53 (0.24 to 0.82) | 1.53 (0.98 to 2.08) |
| | Between 7 and 14 days | Reference | Reference | Reference |
| Chance of complications requiring more time or readmission to hospital | Linear (5–15%) | 0.11 (0.08 to 0.15) | 0.22 (0.17 to 0.26) | 0.49 (0.01 to 0.97) |
| Log-likelihood | −1594 | | | |
| cAIC | 3214 | | | |
| aBIC | 3193 | | | |

Data represent means (95% confidence intervals).

## In relation to other studies

To our knowledge, no previous research has focused on women's preferences for subsequent treatment of an incomplete evacuation of the uterus after misoprostol treatment in first-trimester miscarriage.

Two DCEs were performed among women with a confirmed first-trimester miscarriage (Ryan and Hughes, 1997; Petrou and McIntosh, 2009). Both studies included women who were randomly allocated to expectant, surgical or medical management. *Petrou et al.* designed a questionnaire including six attributes of interest by using literature search. Two attributes (number of days bleeding after treatment and chance of complications requiring more time or readmission to hospital) were similar to our questionnaire and our findings were similar. However, in the study of *Petrou et al.* 'the level of pain experienced' was the most important attribute of interest, which was not considered in the present study. *Ryan and Hughes* designed a questionnaire including five attributes of interest by using the results of their own previous trial which were similar to those used by *Petrou et al. Ryan and Hughes* concluded 'complications following treatment' and 'level of pain

**Table IX Marginal rate of substitution to the chance of more success.**

| % increase in success to accept the undesirable attribute | | | | |
|---|---|---|---|---|
| **Attribute** | **Level** | **Overall** | **Group 1** | **Group 2** |
| Chance of reduced fertility | | 11.2 (8.5 to 13.9) | 8.1 (6 to 10) | 17 (14 to 20) |
| Uncertainty about duration of course | | 1.9 (1.5 to 2.3) | 1.6 (0.9 to 2.3) | 2.8 (2.0 to 3.6) |
| Number of days bleeding after treatment | Between 7 and 14 days instead of 1 day | (0.63 to 1.4) | 0.62 (0.05 to 2.2) | 2 (0.95 to 2.13) |
| | Between 1 and 7 days instead of 1 day | 2.2 (1.1 to 3.3) | 0.81 (0.11 to 1.53) | 2.4 (1.2 to 3.6) |
| Increased chance of complications requiring more time or readmission to hospital | Across range of levels (5–15%) | 5.7 (4.5 to 6.9) | 3.3 (1.8 to 4.8) | 8.5 (6.2 to 11) |

**Table X Two latent-class analysis—patient characteristics.**

| Patient characteristics | Success-driven 41% of women | Risk averse 59% of women | Univariable analysis |
|---|---|---|---|
| Age | 35 (31–39) | 32 (29–35) | 1.03 (0.96–1.08) |
| Previous curettage | 15 | 9 | 2.2 (0.97–4.5) |

Data represent means (95% confidence intervals).

experienced' to be the attributes of interest. Some of these differences in comparison to our study could be explained by using a different approach in designing our DCE. We performed an extensive literature search, expert opinions and interviews with women from the general population, instead of mere literature data.

In contrast, we chose not to include 'the level of pain experienced'. In the literature, a higher level of pain is associated with medical treatment (Nielsen *et al.*, 1996; Johnson *et al.*, 1997; Ngai *et al.*, 2001; Rausch *et al.*, 2012). In this study, we were interested in the preferences for additional treatment (i.e. expectant or surgical management). The level of pain experienced during expectant or surgical management is described in the literature as being equal (Nielsen *et al.*, 1996; Chipchase and James, 1997; Ankum *et al.*, 2001). Therefore, the focus group concluded this was not an attribute of interest in the present study.

In the MisoREST trial 2/3 of the women with a treatment preference, preferred expectant management. In previous research, the most frequently reported reasons for women to prefer medical treatment was the avoidance of surgery and a preference for a more natural process (Molnar *et al.*, 2000; Graziosi *et al.*, 2006). In our study, the attribute 'risk of reduced fertility' was valued the highest and is associated with an expectant management. The MisoREST trial showed that curettage leads to a higher chance of complete evacuation but expectant management was successful in at least 76% of women with an incomplete evacuation of the uterus after medical treatment without leading to more complications. The current research and clinical climates emphasize the importance of informed consent and informed decision making process (Ankum *et al.*, 2001; Wieringa-de Waard *et al.*. 2004; Sotiriadis *et al.*, 2005; Kong *et al.*, 2013).

# Conclusion

Women with an incomplete evacuation of the uterus after misoprostol treatment for miscarriage have strong preferences, whenever subsequent treatment is required. Those treatment preferences are most strongly influenced by 'the risk of a reduced fertility' follow by 'the probability of success'. The highest chance of success would be reached by performing a curettage. However, this bears a relatively high risk of reduced future fertility which is also strongly valued by the study participants. This emphasizes the importance of counselling women about the risk and benefits of all treatment options.

# Supplementary data

Supplementary data are available at *Human Reproduction* online.

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# Authors' roles

JH, MV, ML, WA, BWM and MvW were involved in the conception and design of the study. JH collected the data and drafted the manuscript; MV, ML, WA and BWM carefully reviewed the manuscript. All authors mentioned in the manuscript are members of the MisoREST-trial study group. All authors read, edited and approved the final manuscript.

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# Conflict of interest

None declared.

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