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# Attitudes, satisfaction and experience with administration of progesterone for assisted reproductive treatment

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## ABSTRACT

**METHODS.** Progesterone as luteal phase support is challenging as there is no consensus on whether and how it should be used in different types of fertility treatments, the timing of initiation, dosage, duration of use and form of administration. This study aimed to explore women's attitudes, level of satisfaction and experiences with subcutaneous injection of progesterone (25 mg/day for two weeks) after prior vaginal administration of progesterone in assisted reproductive technology treatments.

**METHODS.** This was a cross-sectional study recruiting women planned for a treatment with progesterone from two public fertility clinics in Denmark. Only women with at least one previous blastocyst transfer using vaginal progesterone were recruited. Questionnaires covered side effects, medication, daily activities, and sex and intimacy.

**RESULTS.** The study had a response rate of 80%, with 100 women participating. Among these, 82% (95% CI: 73-89%) were satisfied (to either a very high or high degree) with the subcutaneous form of their progesterone medication in their current treatment compared with vaginal progesterone in earlier treatments. Furthermore, 84% (95% CI: 75-91%) would choose subcutaneous over vaginal progesterone in future treatments if given the option, whereas 8% (95% CI: 4-15%) preferred the vaginal form.

**CONCLUSIONS.** When comparing experiences with subcutaneous to vaginal administration, our findings showed that subcutaneous progesterone is a suitable alternative for women who are dissatisfied with vaginal administration. If given the opportunity to decide, many would choose the subcutaneous form in future ART treatments.

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Hormonal treatment is highly important for the success of an assisted reproductive technology (ART) treatment. One current focus is the need for progesterone supplementation as luteal phase support. Progesterone is not simple to use as there is no consensus on whether and how it should be used in different types of fertility treatments, or on the timing of initiation, dosage or the duration of use and form of administration [1]. Several forms of progesterone administration are available: vaginal, injectable, rectal or oral. In Denmark, the vaginal route of administration has been the only method used for many years; however, in 2022, subcutaneous injection of progesterone was introduced. RCTs have compared the effects of subcutaneous versus vaginal progesterone during controlled ovarian stimulation (COS). The results were comparable with no difference in implantation, pregnancy, birth and miscarriage rates [2-4]. The same studies found no difference in adverse events, tolerance of and women's satisfaction with the medication [2-4].Focusing on women's satisfaction, Venturella et al.

 

included 69 women with previous experience with vaginal progesterone in a cross-sectional study and found that women undergoing frozen embryo transfer (FET) cycles preferred subcutaneous progesterone administration [5].This study aimed to explore women's attitudes towards, level of satisfaction and experiences with subcutaneous injection of progesterone (25 mg/day for two weeks) after prior vaginal progesterone administration in ART treatments.

## Methods

This was a cross-sectional study recruiting women from the Fertility Clinic at Copenhagen University Hospital-Herlev and Gentofte and the Fertility Unit at Aalborg University Hospital from March 2022 to June 2023.

Women undergoing ART treatment were included in the following treatments: 1) In COS cycles covering both standard long agonist and short antagonist protocols with either recombinant follicle-stimulating hormone or highly purified menotropin. When the leading follicles reached 17-18 mm, ovulation was induced with administration of human chorionic gonadotropin (hCG), and after 34-36 hours, the oocyte pick up (OPU) was performed. Progesterone administration was initiated the day after OPU and used for approximately two weeks. 2) For FET treatments, women with regular menstrual cycles underwent modified natural FET cycles with ovulation induction with hCG and using progesterone for approximately two weeks [1].

All women were recruited based on the following inclusion criteria: 1) age 18-45 years, 2) ability to understand and read Danish, 3) at least one previous transfer using a vaginal application of progesterone (vaginal tablet three times/day, gel once/day, or vagitory twice/day) and 4) starting ART treatment where progesterone was planned for luteal phase support. Women with the following criteria were excluded: 1) first in vitro fertilisation/intracytoplasmic sperm injection cycle, 2) first FET cycle with no previous transfer following COS treatment, and 3) known allergy towards progesterone preparations. To ensure that all women had gained experience (two weeks) in using the medication and were not affected by the result of the pregnancy test, they were asked to complete the questionnaire one day prior to the planned pregnancy test, which is normally performed 10-11 days after embryo transfer.

### Data collection

If the physician had prescribed subcutaneous progesterone, clinic research nurses gave information, orally and in writing (Supplementary material), about the study during the women's attendance at the fertility clinic. If a woman decided to participate, she had to provide oral and written informed consent. When starting a fertility treatment in Denmark, there is a threshold limit on patients' payment for medication. Beyond this level, medication is fully subsidised. In this study, medication costs were covered in accordance with usual practice. Women who participated and those who did not received the same guidance on how to use the medication. The standard progesterone prescription at the two participating fertility clinics was vaginal administration. If Prolutex was prescribed, this was at the treating physician's discretion. The questionnaire was based on existing literature [5-7] and was validated for face and content validity, with clarity assessed by clinical colleagues and linguistic and conceptual aspects reviewed by the authors. Using the Research Electronic Data Capture (REDCap) web platform [8, 9], participants were sent a personal link to the questionnaire. The questionnaire was divided into the following sections, with questions in all sections given to all participants: Side effects, Medication, Daily activities, Travel activities, Sex and intimacy, Summary questions, Comparative questions and Questions on participant characteristics. Additional questions depended on the preceding answer. For example, only participants who responded yes to having had intercourse or being intimate were asked additional questions related to this topic. Participants who responded *Low degree* or *Very low degree* to a question had the opportunity to elaborate in free text about the reasons for their answers. The response categories were defined

 

as follows: *Yes, No* and *Do not know*. *Injection into the skin, Vaginal application* and *Do not know*. 1, *Very high degree*, 2, *High degree*, 3, *Appropriate degree*, 4, *Low degree*, 5, *Very low degree*, 6, *Do not know*. 1, *Much better subcutaneously*, 2, *Better subcutaneously*, 3, *Similar*, 4, *Better vaginally*, 5, *Much better vaginally*, 6, *Do not know* (Supplementary material).

**Data analysis**

For questions with six response categories, the percentage of respondents who answered each category was calculated, along with 95% CI for the main results. Means with SD and 95% CI were calculated where appropriate. Before calculating mean estimates, the response category 'Do not know' was removed. Questions that could be elaborated on in free-text responses were sorted and summarised. We performed additional analyses stratifying all estimates by the number of previous embryo transfers (1, ≥ 2 transfers). Data analysis was performed with the statistical software R, version 4.1.2 [10].

**Ethics**

The study was approved by the Danish Data Protection Agency. The two clinics entered into a Data Processing Agreement (R.no.: P-2021-501, version 3.1.) regarding the data controllers' processing of the data. Under Danish law, no approval was required from the regional ethics committee.

*Trial registration:* none.

## Results

A total of 230 women were invited to participate; 78 declined, 26 did not participate due to cancelled blastocyst transfer, and one withdrew her informed consent. The questionnaire was sent to 125 women, of whom 100 completed it, yielding a response rate of 80% (Supplementary material). In all, 42 had a COS treatment, and 58 underwent a modified natural FET cycle (**Table 1**).

**TABLE 1** Sociodemographic and medical characteristics of the study population.

| | |
|---|---|
| *Participants, n* | |
| Herlev Hospital | 42 |
| Aalborg University Hospital | 58 |
| Total | 100 |
| Age, mean, (SD) [range], yrs | 33 (4.5) [20-41] |
| *Place of birth, n* | |
| Europe | 95 |
| Africa | 1 |
| Asia | 4 |
| *Place of growing up, n* | |
| Europe | 97 |
| Africa | 1 |
| Asia | 2 |
| *Education, n* | |
| No education | 1 |
| Student | 2 |
| Short higher education: 1-2 yrs | 21 |
| Medium higher education: 3-4 yrs | 47 |
| Long higher education: ≥ 5 yrs | 29 |
| BMI, mean, (SD) [range], kg/m$^2$ | 25 (4.1) [18-35] |
| *Type of treatment, n* | |
| COS | 42 |
| FET: modified natural | 58 |
| *Vaginal bleeding after embryo transfer, n* | |
| Yes | 31 |
| No | 68 |
| Do not know | 1 |
| *Previous oocyte pick-ups, n* | |
| 1 | 46 |
| 2 | 27 |
| 3 | 18 |
| ≥ 4 | 9 |
| Do not know | 0 |
| *Previous embryo transfers, n* | |
| 1 | 36 |
| 2 | 16 |
| 3 | 19 |
| ≥ 4 | 28 |
| Do not know | 1 |

COS = controlled ovarian stimulation; FET = frozen embryo transfer.

### Side effects

A total of 23% of the women reported being informed about potential side effects of subcutaneous progesterone, whereas 64% reported experiencing side effects during treatment with subcutaneous progesterone (**Table 2**).

**TABLE 2** Attitudes, satisfaction and experiences related to side effects, medication, daily activities, travel activities, sex and intimacy, and summary questions following subcutaneous administration of progesterone. Response categories: very high degree, high degree, appropriate degree or similar, low degree, very low degree are rated on a 1-5 scale. The "Do not know" category only appears in this table if it was checked. In all analyses, "Do not know" was removed.

| | % (n) | Mean (SD) [95% CI] |
|---|---|---|
| *Side effects* | | |
| Were you informed about any side effects to the progesterone medication during this treatment? | | |
| Yes | 23 (23) | [52-72%] |
| No | 62 (62) | [15-32%] |
| Do not know | 15 (15) | |
| Have you experienced any side effects to your progesterone medication during this treatment? | | |
| Yes | 64 (64) | [54-73%] |
| No | 25 (25) | [17-35%] |
| Do not know | 11 (11) | |
| *Medication* | | |
| To what degree are you satisfied with the form of administration of progesterone during this treatment compared with your previous treatment? | | 1.81 (0.93) [1.63-1.99] |
| Very high + high degree | 82 (82) | |
| Appropriate degree | 11 (11) | |
| Low + very low degree | 7 (7) | |
| To what degree during this treatment has it been possible to take your progesterone medication exactly as you had been informed to do? | | 1.59 (0.74) [1.44-1.73] |
| Very high + high degree | 86 (86) | |
| Appropriate degree | 12 (12) | |
| Low + very low degree | 1 (1) | |
| Do not know | 1 (1) | |
| To what degree were you sure during this treatment that you had taken your progesterone medication correctly? | | 1.74 (0.75) [1.59-1.89] |
| Very high + high degree | 83 (83) | |
| Appropriate degree | 15 (15) | |
| Low + very low degree | 1 (1) | |
| Do not know | 1 (1) | |
| To what degree during this treatment have you been sure that you have received the full dose of your progesterone medication? | | 2.02 (0.90) [1.84-2.20] |
| Very high + high degree | 66 (66) | |
| Appropriate degree | 29 (29) | |
| Low + very low degree | 4 (4) | |
| Do not know | 1 (1) | |
| To what degree during this treatment was it possible for you to remember to take your progesterone medication? | | 1.31 (0.51) [1.21-1.41] |
| Very high+ high degree | 98 (98) | |
| Appropriate degree | 2 (2) | |
| Low + very low degree | 0 (0) | |
| To what degree during this treatment was it possible for you to store your medication correctly? | | 1.43 (0.62) [1.31-1.55] |
| Very high degree | 95 (95) | |
| Appropriate degree | 4 (4) | |
| Low + very low degree | 1 (1) | |
| To what degree during this treatment was it possible for you to take your progesterone medication yourself? | | 1.59 (1.05) [1.38-1.79] |
| Very high + high degree | 89 (89) | |
| Appropriate degree | 3 (3) | |
| Low + very low degree | 7 (7) | |
| Do not know | 1 (1) | |
| During this treatment did you ever forget to take your progesterone medication? | | |
| Yes | 6 (6) | |
| No | 94 (94) | |

Continues >

**TABLE 2 (CONTINUED)** Attitudes, satisfaction and experiences related to side effects, medication, daily activities, travel activities, sex and intimacy, and summary questions following subcutaneous administration of progesterone. Response categories: very high degree, high degree, appropriate degree or similar, low degree, very low degree are rated on a 1-5 scale. The "Do not know" category only appears in this table if it was checked. In all analyses, "Do not know" was removed.

| | % (n) | Mean (SD) [95% CI] |
|---|---|---|
| What did you do when you realised that you had forgotten to take your progesterone medication? | | |
| Did not take it | 33 (2) | |
| Took it but delayed | 50 (3) | |
| Contacted the fertility clinic | 17 (1) | |
| Contacted my general practitioner | 0 (0) | |
| Contacted on-call doctor | 0 (0) | |
| Other | 0 (0) | |
| *Daily activities* | | |
| To what degree during this treatment was it possible to bring your next dose of progesterone medication with you in connection with your daily activities? | | 1.93 (0.98) [1.73-2.12] |
| Very high + high degree | 65 (65) | |
| Appropriate degree | 23 (23) | |
| Low + very low degree | 6 (6) | |
| Do not know | 6 (6) | |
| To what degree could you take your progesterone medication during this treatment without it affecting your working day/daily life | | 1.68 (0.76) [1.53-1.83] |
| Very high + high degree | 84 (84) | |
| Appropriate degree | 15 (15) | |
| Low + very low degree | 1 (1) | |
| To what degree during this treatment was it possible to take your progesterone medication without it affecting your leisure time? | | 1.75 (0.83) [1.59-1.91] |
| Very high + high degree | 79 (79) | |
| Appropriate degree | 19 (19) | |
| Low + very low degree | 2 (2) | |
| *Travel activities* | | |
| Have you been on a trip or been travelling while taking your progesterone medication in this treatment? | | |
| Yes | 25 (25) | |
| No | 75 (75) | |
| To what degree during this treatment was it possible to take your progesterone medication with you on trips and travels? | | 1.84 (0.94) [1.66-2.02] |
| Very high + high degree | 72 (18) | |
| Appropriate degree | 24 (6) | |
| Low + very low degree | 4 (1) | |
| *Sex and intimacy* | | |
| Have you had intercourse/been intimate while taking your progesterone medication during this treatment? | | |
| Yes | 37 (37) | |
| No | 63 (63) | |
| To what degree during this treatment could you take progesterone medication without it interfering with intercourse/intimacy? | | 1.43 (0.77) [1.28-1.58] |
| Very high + high degree | 89 (33) | |
| Appropriate degree | 8 (3) | |
| Low + very low degree | 3 (1) | |
| To what degree during this treatment could you and your partner have intercourse/be intimate without your partner being bothered by your progesterone medication? | | 1.19 (0.40) [1.11-1.23] |
| Very high + high degree | 100 (37) | |
| Appropriate degree | 0 (0) | |
| Low + very low degree | 0 (0) | |
| To what degree during this treatment could you take your progesterone medication without it affecting your sexual pleasure when you and your partner had intercourse/were intimate? | | 1.42 (0.69) [1.28-1.55] |
| Very high + high degree | 86 (32) | |
| Appropriate degree | 11 (4) | |
| Low + very low degree | 0 (0) | |
| Do not know | 3 (1) | |

Continues >

**TABLE 2 (CONTINUED)** Attitudes, satisfaction and experiences related to side effects, medication, daily activities, travel activities, sex and intimacy, and summary questions following subcutaneous administration of progesterone. Response categories: very high degree, high degree, appropriate degree or similar, low degree, very low degree are rated on a 1-5 scale. The "Do not know" category only appears in this table if it was checked. In all analyses, "Do not know" was removed.

| | % (n) | Mean (SD) [95% CI] |
|---|---|---|
| To what degree during this treatment could you take your progesterone medication without it affecting your sexual desire, before or when you and your partner had intercourse/were intimate? | | 1.94 (0.92) [1.76-2.13] |
| Very high + high degree | 64 (24) | |
| Appropriate degree | 30 (11) | |
| Low + very low degree | 3 (1) | |
| Do not know | 3 (1) | |
| *Summary questions* | | |
| To what degree do you prefer your current progesterone medication compared with your previous progesterone medication? | | 1.70 (0.98) [1.51-1.90] |
| Very high + high degree | 81 (81) | |
| Similar | 9 (9) | |
| Low + very low degree | 7 (7) | |
| Do not know | 3 (3) | |
| To what degree does your current progesterone medication take longer to take than your previous progesterone medication? | | 3.66 (1.13) [3.44-3.89] |
| Very high + high degree | 18 (18) | |
| Similar | 27 (27) | |
| Low + very low degree | 53 (53) | |
| Do not know | 2 (2) | |
| To what degree is your current progesterone medication easy and simple to administer? | | 2.29 (0.94) [2.11-2.47] |
| Very high + high degree | 57 (57) | |
| Similar | 35 (35) | |
| Low + very low degree | 8 (8) | |
| To what degree can you manage your current progesterone medication without experiencing it as being stressful? | | 2.03 (0.88) [1.86-2.20] |
| Very high degree | 73 (73) | |
| Similar | 22 (22) | |
| Low + very low degree | 5 (5) | |
| If you had to choose for yourself, which progesterone medication would you choose for future treatment? | | |
| Injection into the skin | 84 (84) | [75-91%] |
| Vaginal application | 8 (8) | [4-15%] |
| Do not know | 8 (8) | |

### Medication

The results showed that most women were more satisfied with the subcutaneous form of administration of their progesterone medication in this treatment than with vaginal administration in the last treatment; 45% to a very high degree, 37% to a high degree, 11% to an appropriate degree, 6% to a low degree and 1% to a very low degree. If the women were given the opportunity to decide the administration form for a future progesterone medication, 84% would choose subcutaneous administration, 8% vaginal administration and 8% did not know (Table 2).

In questions related to the treatment with subcutaneous progesterone that focused on *medication,* i.e. *"To what degree are you satisfied with the form of administration of progesterone during this treatment compared with the last treatment?",* the mean score was 1.81, indicating a high level of satisfaction with subcutaneous administration (1 indicating a very high degree and 5 a very low degree). In cases where women were not satisfied, reasons for dissatisfaction included the quality of the syringes and trouble puncturing the skin with the needle, making it difficult to make the injection, and causing considerable soreness.

### Daily activities

One question focused on the current treatment and *daily activities: "To what degree during this treatment was it possible to bring your next dose of progesterone medication with you in connection with your daily activities?"* The mean score of 1.93 indicates a high likelihood. In cases where women were unable to bring the progesterone, they pointed out that more equipment was involved in subcutaneous injections and described problems with the storage of used needles.

**Travel activities**

A total of 25 women participated in travel activities during their treatment. One question related to the current treatment, focusing on *travel activities: "To what degree during this treatment was it possible to take your progesterone medication with you on trips and travels?"* A mean score of 1.84 indicated a high likelihood. In cases where women were not satisfied, they indicated, for example, problems with ensuring a suitable hygiene standard while travelling.

**Sex and intimacy**

A total of 37 women have had intercourse/been intimate while taking subcutaneous progesterone. One question focused on sex and intimacy: *"To what degree during this treatment could you take progesterone medication without it interfering with intercourse/intimacy?"* The mean score was 1.43, indicating a low degree of interference. In cases where women were not satisfied, they reported, for example, that they felt bloated and uncomfortable from the treatment (Table 2 and **Table 3**).

**TABLE 3** Summary of elaborations from the questionnaire. Participants who responded "low degree" or "very low degree" to a question had the opportunity to elaborate in free text on the reasons for their responses.

| Section in questionnaire | Summary of elaborations |
|---|---|
| Side effects | Reported side effects included soreness, redness, itching, irritation, lumps, bruising, burning, skin reactions and general discomfort at the injection site<br>Systemic side effects such as breast soreness, fatigue, headache, nausea, bloating, constipation, abdominal discomfort, mood swings, acne, spotting and bleeding were also reported |
| Medication | Dissatisfaction was linked to poor syringe quality, pain during injection, dosage uncertainty and loss of medication due to air bubbles or preparation issues<br>Some respondents were confused about vial content, had problems with storage and depended on partners because they disliked self-injection |
| Daily activities | Challenges included transporting used needles, messy storage and the injection process being more complex than vaginal alternatives<br>Several preferred to inject only at home, depended on others for help, struggled with strict timing and found haematomas limiting for movement |
| Trips and travels | The main challenge when travelling was maintaining hygiene and safely handling used needles |
| Sex and intimacy | Feeling bloated and uncomfortable was reported, which bothered intimacy |
| Summary question | Overall, the progesterone injections were experienced as painful, stressful and complicated<br>Compared with vaginal alternatives, the treatment was seen as more burdensome due to equipment issues, injection-related pain, uncertainty about dosage and the dependency it created in daily routines |

### Summary questions

The *summary questions* showed mean scores of 1.70-3.66, generally indicating a high degree of satisfaction with subcutaneous progesterone (Table 2).

Comparing subcutaneous with vaginal administration in relation to eight areas, with the response categories 1, *Much better subcutaneous* to 5, *Much better vaginal* showed mean scores of 1.18-2.53, describing a trend towards a preference for subcutaneous progesterone treatment (**Table 4**). For all analyses, stratification on the number of previous transfers yielded comparable results.

**TABLE 4** Comparison of experiences with subcutaneous and vaginal progesterone administration.

| | 1-6 scale, % (95% CI) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 point: Subcutaneous is much better | 2 points: Subcutaneous is better | 3 points: Similar | 4 points: Vaginal is better | 5 points: Vaginal is much better | 6 points: Do not know | Points, mean (SD) [95% CI] |
| Form of administration | 42 (32-52) | 32 (23-42) | 13 (7-21) | 7 (3-14) | 3 (0.6-8) | 3 (0.6-8) | 1.94 (1.07) [1.73-2.15] |
| Discomfort | 29 (20-39) | 35 (26-45) | 13 (7-21) | 13 (7-21) | 7 (3-14) | 3 (0.6-8) | 2.32 (1.24) [2.07-2.57] |
| Side effects | 20 (13-29) | 26 (18-36) | 24 (16-34) | 14 (8-22) | 5 (2-11) | 11 (6-19) | 2.53 (1.17) [2.29-2.77] |
| Medication administration per day | 84 (75-91) | 12 (6-20) | 3 (0.6-8) | 0 | 0 | 1 (0.03-5) | 1.18 (0.46) [1.09-1.27] |
| *Daily activities* | | | | | | | |
| Job/studies | 59 (49-69) | 22 (14-31) | 12 (6-20) | 3 (0.6-8) | 0 | 4 (1-9) | 1.57 (0.83) [1.41-1.74] |
| Leisure time | 57 (47-67) | 23 (15-32) | 11 (6-19) | 6 (2-13) | 0 | 3 (0.6-8) | 1.65 (0.91) [1.47-1.83] |
| Travel activities | 42 (32-52) | 15 (0.9-24) | 17 (10-26) | 6 (2-13) | 0 | 20 (13-29) | 1.84 (1.01) [1.62-2.06] |
| Sex and intimacy | 59 (49-69) | 20 (13-29) | 5 (2-11) | 1 (0.03-5) | 0 | 15 (0.9-24) | 1.39 (0.66) [1.25-1.53] |

## Discussion

The results showed that a substantial proportion of the women were satisfied with subcutaneous progesterone administration during their current treatment compared with vaginal administration in earlier treatments. If they were given the opportunity to decide, most would choose subcutaneous administration.

Previous RCTs have reported no difference in women's satisfaction when comparing two different routes of administration [2-4]. The present study differs from previous RCTs since it was a cross-sectional study, allowing inclusion of women with prior experience with vaginal luteal-phase support and assessing their satisfaction following subcutaneous injection. A similar design was used by Venturella et al., who included patients in FET cycles [5]. This study included patients in both COS and FET cycles.

It is well documented that infertility has an extensive psychological impact on women's lives. Women undergoing fertility treatment may be concerned about intimacy and their relationship with their partner. Anxiety, anger, depressed mood and cognitive impairment are described to be associated with infertility [11-13]. Since fertility treatment can be highly difficult at a personal and relationship level, all possible areas for a reduction of this burden must be considered. Our results show that some women prefer subcutaneous progesterone administration. Perhaps the choice of administration form for the luteal-phase support could be an opportunity to reduce potential difficulties.

The decision regarding and the prescription of medicine for the woman lie with the attending physician. Our finding that 84% of the women would choose subcutaneous progesterone if they were given the opportunity to decide is interesting. This result shows that women have an opinion about which type of hormone administration they prefer, and our results suggest that they should be included in the decision-making process when different administration types are available. It is well known that patient-centred care during infertility healthcare provision encourages well-being during treatment [14]. Many women are interested in and actively request individualised treatment, and there is a growing focus on how to provide such personalised treatment that meets their specific needs for progesterone. Involving women in choosing the administration form could

support individualised treatment and well-being.

When investigating different forms of administration, participating women must have experience with both subcutaneous and vaginal progesterone, which was a strength of this study. Furthermore, the inclusion of women from two different fertility clinics undergoing both COS and FET treatment and the variation regarding age and education enhances the generalisability of the present results. Another strength is the equal 14-day comparison of subcutaneous and vaginal progesterone. A limitation could be the risk of recall bias, since the most recent treatment with subcutaneous progesterone would be easier to remember. It could be argued that it is unlikely that the physician would prescribe subcutaneous progesterone to patients with a fear of needles when a vaginal administration was available or to those who specifically requested vaginal administration, which might introduce selection bias. Furthermore, comparing previously unsuccessful cycles following vaginal administration with the subcutaneous administration in a cycle where there are new hopes and an unknown outcome could be considered a limitation. However, covering daily life and completing the questionnaire before the pregnancy test is a strength. It could be seen as a limitation that 78 women declined to participate, and 25 did not respond, as non-responders are less likely to be satisfied than responders are [15]. However, a 65% response rate is considered acceptable [16], and the actual response rate of 80%, which is well above the acceptable response rate, should be considered a strength.

## Conclusions

This study showed that subcutaneous progesterone is a suitable alternative for women who are dissatisfied with vaginal administration. When asking women to compare subcutaneous administration in an ongoing treatment with earlier treatments with vaginal administration across eight areas, we found a trend towards preferring subcutaneous administration, although some women preferred vaginal administration. The majority of women would choose subcutaneous progesterone if given the option after using both forms.

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**References** can be found with the article at ugeskriftet.dk/dmj

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**Supplementary material** https://content.ugeskriftet.dk/sites/default/files/2025-11/supplementary_a05250447.pdf

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