# **Original Article**

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# Complementary and alternative medicine among women and men prior to and during fertility treatment

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# ABSTRACT

**INTRODUCTION** The use of complementary and alternative medicine (CAM) is generally increasing. CAM use in relation to fertility treatment is sparsely studied. Thus, the aim of this study was to assess the use prevalence and patterns of CAM among Danish women and men initiating or receiving fertility treatment. Additionally, we aimed to establish whether several fertility treatment attempts influenced CAM use prevalence.

**METHODS** A cross-sectional survey was conducted at the second largest fertility clinic in Denmark in the period from April to June 2018. The CAM use prevalence was reported for two groups of patients. Specifically, CAM use prior to or during fertility treatment was compared between groups, and various general patterns were reported.

**RESULTS** Among the 411 patients approached, 277 responded (67.4%). Among these patients, 142 participants had not previously received fertility treatment, whereas 135 participants had received treatment at least once previously. We found that 52.5% of the patients initiating and undergoing fertility treatment had used CAM. Furthermore, previous fertility treatment was related to a higher CAM use. Surprisingly, only 53.4% of the participating women used folic acid.

**CONCLUSIONS** More than half of the women and men initiating or undergoing fertility treatment had been using the investigated CAM. Of notice, folic acid compliance was low. The frequency of CAM use increased during fertility treatment.

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Complementary and alternative medicine (CAM) is used worldwide for a variety of purposes. Studies have shown that the global use of herbal medicine has increased among specific patient groups, including patients with cardiovascular and rheumatic diseases, pregnant and menopausal women and patients with psychological diseases [1-5]. Some patients use CAM to prevent disease; others to benefit from the treatment or to avoid unsatisfactory effects of conventional treatments [6]. However, this area has only been sparsely studied and more research into the effect of CAM in general and in relation to fertility treatment in particular is needed [7].

CAM comprises a variety of different types of vitamins, minerals and other supplements. Folic acid is the only recommended supplement before and during pregnancy, partly because it prevents birth defects, partly because it improves the chance of achieving and maintaining a pregnancy [8]. Use of other CAM and herbal medicines during pregnancy has been studied only sparsely, and some types of CAM have been identified as being potentially harmful [9]. Thus, the purpose of this study was to assess the prevalence and patterns of CAM use among Danish women and men initiating or receiving fertility treatment. Additionally, the study evaluated whether several fertility treatment attempts influenced the prevalence of CAM use.

# METHODS

#### Study setting and participants

All women and men referred for in vitro fertilisation (IVF) treatment in the second largest Danish public fertility clinic at Horsens Regional Hospital from April to June 2018 were invited to attend a general information meeting prior to their first fertility treatment. Furthermore, for two weeks, all women and men visiting the outpatient clinic for a treatment appointment - e.g., their second stimulation - were invited to participate. The only exclusion criterion was language challenges as non-Danish speaking patients may not be able to complete the survey independently.

#### Study instrument

A cross-sectional survey was conducted to evaluate the use prevalence of complementary vitamins, minerals, herbs and alternative treatment. The definition of CAM varies in the literature. In this study, we defined CAM as follows: vitamins and minerals, omega-3 fatty acids, herbs and alternative treatment. Herbs comprised St. John's Wort, valerian, ginger, kava, ginseng, pomegranate and others. Alternative treatment comprised reflexology, acupuncture, craniosacral therapy, massage, mindfulness and osteopathy. The survey consisted of questions concerning demographic characteristics, fertility treatment and information about CAM. Demographic characteristics including age, gender, level of education, occupational status and civil status were also obtained.

#### Data collection and statistical analysis

Data were collected in RedCap - a secure web application for building and managing surveys with proper and safe information processing ensuring anonymity.

Statistical analyses were performed in EpiBasic - a tool for statistical analysis of tabular information. The  $\chi^2$ -test was used for comparison of the use prevalence of vitamins, minerals, herbs and alternative treatment between the two groups of patients prior to or during fertility treatment. A *p*-value < 0.05 was considered statistically significant.

Trial registration: not relevant.

#### RESULTS

In total, 411 women and men were invited to participate. Among those invited, 277 participants accepted and were enrolled in the study, yielding a 67.4% total response rate. Among the enrolled patients, 243 were seen in relation to their first referral for fertility treatment, and 168 of the women and men were seen while attending the outpatient clinic. In total, 251 women and men were invited for the information meeting of whom 125 consented to participating. In the outpatient clinic, 160 women and men were invited and 152 consented to participating.

#### Demographic data

The demographics of the studied groups are presented in **Table 1**. In total, 277 patients participated, 191 women and 86 men. Among the 277 participants, 142 had not previously received fertility treatment (51.3%, 96 women and 46 men), whereas 135 had received at least one treatment (48.7%).

Characteristicst	No previous fertility treatment (n = 142 (51.3%))	Previous fertility treatment (n = 135 (48.7%))	p-value
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Age			
< 20 yrs	-	-	-
20-24 yrs	4.9	2.2	0.24
25-29 yrs	21.1	30.4	0.18
30-34 yrs	40.9	29.6	0.18
35-37 yrs	16.2	18.5	0.67
38-40 yrs	11.9	15.6	0.45
> 41 yrs	4.9	3.7	0.63
Gender: female	71.1	66.3	0.83
Education			
Primary school	2.1	3.7	0.44
High school	12.7	5.9	0.08
Education lasting ≤ 2 yrs	13.4	15.6	0.66
Education lasting 3-4.5 yrs	40.9	53.3	0.21
Education lasting ≥ 5 yrs	31.0	21.5	0.17
Occupational status: working	85.2	82.2	0.84
Civil status: in relationship	91.5	89.6	0.90

# TABLE 1 Demographic data on participants (N = 277). The values are %.

The age distribution within the two studied groups was nearly identical with most of the participants being 25-34 years of age in both groups. The only significant difference was that the group of participants who had not previously received fertility treatment had a significantly higher proportion of participants aged 30-34 years (p < 0.05) than participants who had received fertility treatment previously. Regarding level of education, most participants in the two study groups had an education lasting three to four and a half years, or a minimum of five years. The majority were in a relationship and employed.

# Overall use of complementary and alternative medicine

Overall, 52.5% (n = 145) of women and men reported using vitamins, minerals, herbs and/or alternative treatment. The use prevalence was significantly higher among women than among men; 78.6% (n = 114) and 21.4% (n = 31), respectively (p < 0.02).

# Use of vitamins and minerals

The use of vitamins and minerals is presented in **Table 2**. The prevalence in the two groups ranged from 7.8% to 45.2% depending on the types of vitamins and minerals used. In general, the use prevalence of vitamins and minerals was higher among participants who had previously received fertility treatment than among participants initiating fertility treatment, although this difference did not reach statistical significance. The only exception was vitamin A (Table 2).

	No previous fertility treatment (n = 142 (51.3%))	Previous fertility treatment (n = 135 (48.7%))	Difference (95% CI)	p-value
Vitamin A	38.0	31.1	6.9 (-18.1-4.3)	0.23
Vitamin B	13.4	16.3	2.2 (-5.5-11.3)	0.49
Vitamin C	11.3	11.9	0.6 (-7.0-8.1)	0.88
Vitamin D	23.9	27.4	3.5 (-6.8-13.8)	0.51
Vitamin E	7.8	10.4	2.6 (-4.1-9.4)	0.44
Combined vitamin supplement	37.3	45.2	7.9 (-3.7-19.4)	0.18
Selenium	9.9	13.3	3.5 (-4.1-11.0)	0.37
Zinc	12.7	15.6	2.9 (-5.3-11.1)	0.49
Magnesium	14.1	20.0	5.9 (-2.9-14.8)	0.19
Folic acid	35.2	42.2	7.01(-4.4-18.5)	0.23
Fish oil	26.8	30.4	3.61 (-7.0-14.3)	0.51
CI = confidence interval.				

**TABLE 2** Results on the use of vitamins and minerals among participants (N = 277). The values are %.

Folic acid was reported by 53.4% (n = 102) of all women. The prevalence was higher among women who had previously received fertility treatment (59.4%) than among women initiating fertility treatment (47.4%), but this difference was not significantly significant (p = 0.10).

# Use of herbs

The use prevalence of herbs was significantly higher among participants who had previously received fertility treatment (20.8%, n = 28) than among participants who had never received fertility treatment (9.2%, n = 13), (p < 0.04). Furthermore, the use was higher among women (15.7%, n = 30) than among men (10.9%, n = 9), but this difference was not statistically significant (p = 0.25). The most frequently used herb was ginger. Thus, 4.2% (n = 6) of the participants who had not received fertility treatment previously and 8.2% (n = 11) of the participants who had received fertility treatment previously used ginger (p = 0.17).

# Use of alternative treatment

A total of 27.4% (n = 37) of the participants who had previously received fertility treatment used alternative treatment. This percentage was significantly higher than the 16.9% (n = 29, p < 0.049) of the participants who had not received fertility treatment previously (**Table 3**). Again, women used alternative treatment significantly more frequently (29.8%, n = 57) than men (3.5%, n = 3, p < 0.001). Depending on the type of alternative treatment, we found that the use prevalence of each type ranged from 0.7% to 17.8%, with acupuncture being the most used treatment. For details, see Table 3. Statistical analyses were conducted (Table 3), but the low prevalence in this group should be taken into account when interpreting these results.

	No previous fertility treatment (n = 142 (51.3%))	Previous fertility treatment (n = 135 (48.7%))	Difference (95% Cl)	p-value
Reflexology	2.8	11.1	8.3 (2.3-14.3)	0.006
Acupuncture	4.2	17.8	14.9 (7.9-21.9)	0.0003
Craniosacral therapy	0.7	2.2	1.5 (-1.3-4.4)	0.29
Massage	4.9	10.4	5.4 (-0.8-11.7)	0.09
Mindfulness	6.3	8.9	2.6 (-3.7-8.8)	0.42
Osteopathy	1.4	4.4	3.0 (-0.9-7.0)	0.32
CI = confidence interval.				

**TABLE 3** Results on the use of alternative treatment among participants (N = 277). The values are %.

#### Pattern in the use of complementary and alternative medicine

When investigating the CAM use prevalence stratified by level of education, we compared participants having primary school as the highest attained educational level to participants with high school, an education lasting two years, 3-4.5 years or a minimum of five years. We found an increasing use prevalence with a higher level of education (from around 2% to 50%). The only exception was participants who had an education lasting a minimum of five years, among whom only an average of 25% used CAM.

No difference was observed in the CAM use prevalence when exploring civil status, occupational status or age groups.

#### DISCUSSION

#### Main findings

To our knowledge, this is the first study to investigate the use of CAM in patients attending a fertility clinic in Denmark. We found that 52.5% (n = 145) of women and men reported using vitamins, minerals, herbs and/or alternative treatment. The use frequency was higher among women than among men, which is also reported by other studies [10, 11]. The use increased if the patients had previously received fertility treatment. This trend was also reported in a South Korean study [12]. In concordance with other studies [10, 13], the use prevalence was also higher for participants who had attained education above the primary school level, and the use prevalence increased with increasing level of education.

#### Complementary and alternative medicine use and infertility

The use prevalence of CAM in patients with infertility has only been sparsely investigated.

This study implied that CAM use is relatively high (52.5%) overall. Other studies estimated that 20-44.7% of patients used CAM for their infertility [14, 15].

Notably, only 53.4% (n = 102) of all women reported consuming folic acid. This prevalence is substantially lower than expected considering that folic acid supplements are recommended both before and during pregnancy as they may prevent birth defects while improving the chance of achieving and maintaining pregnancy [16]. The low folic acid compliance observed was in line with the compliance reported in other studies (42-65.7%) [11, 17].

#### Pattern in complementary and alternative medicine use in Denmark

In Denmark, the CAM use prevalence in the general population has only been sparsely studied. The CAM use prevalence among pregnant women was found to fall in the 4-69% range [13, 18]. We found herb use prevalence to be 9.2% and 20.7% prior to and during fertility treatment, respectively. However, comparing data requires a more precise definition of the investigated herbs.

Regarding alternative treatment, we found that 27.4% of participants who had received fertility treatment previously used alternative treatment. In contrast, the prevalence in participants who had never received fertility treatment was 16.9%. Other studies have found that the use prevalence of alternative treatment ranged from 20% to 45% in other patient groups [11, 19]. Generally, comparing data from other studies is difficult as study design, CAM definition and local CAM use patterns differ among studies.

# Strengths and limitations of the study

The strengths of this study include a rather large study group and a 67.4% response rate, reducing the risk of response bias. Furthermore, the study is likely generalizable as Danish Healthcare provides insemination and up to three IVF stimulations with transfers being readily and equally available to all women in Denmark free of charge. Thus, selection bias is limited as women from all social classes were offered the same treatment options.

One limitation is that most of the participants were Danish-speaking Caucasians. Thus, knowledge about CAM use in non-Danish speaking, non-Caucasian patients is lacking. Furthermore, the risk of recall bias may be a limitation. In the present study, participants had to remember their use of CAM within the past three months or more. Answering the survey online may provide a more precise indication of the real consumption than a stressful situation at the outpatient clinic.

# Implication of the findings and further studies

Further research is needed to investigate the extent of CAM use for fertility enhancement. As CAM varies in both frequency and contents between cultures, each fertility clinic should be aware of its local patterns to optimize the fertility treatment and guidance of the patients.

An enhanced focus on information about folic acid supplements to prevent birth defects is urgently needed based on the low use prevalence of folic acid in this study. In general, Danish Healthcare has very limited focus on CAM, and few patients inform their doctors of their CAM use [13, 20].

The high CAM use frequency reported herein underpins the need for further investigation of the efficacy and safety of alternative medicine use during fertility treatment, especially as the quality of the evidence across CAM methods during fertility treatment is poor [7].

# CONCLUSIONS

More than half of the Danish women and men initiating and undergoing fertility treatment in this study had been using the investigated CAM within the past three months. Participants who had received fertility treatment previously recorded a significantly higher use of alternative treatment and herbs than participants who had not previously received fertility treatment. Women had a significantly higher use of alternative treatment and herbs than men. However, only about half of the Danish women consumed the recommended folic acid supplementation. This topic urgently needs more attention as folic acid supplementation has been proven to reduce birth defects. Furthermore, the fact that the frequency of CAM use increased during treatment underpins the need for further investigation of the safety of complementary and alternative medicine use during fertility treatment. Correspondence Anne Dige Soegaard. E-mail: annesoegaard@hotmail.com

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