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The Fertility Assessment and Counseling Clinic – does the concept work? A prospective 2-year follow-up study of 519 women

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Conflict of interest
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Abstract

Introduction. The Fertility Assessment and Counseling (FAC) Clinic was initiated to provide women with information about their current fertility status to prevent infertility and smaller families than desired. The aim was to study the predictive value of a risk assessment score based on known fertility risk factors in terms of time to pregnancy. *Material and methods.* Prospective cohort study of the first 570 women attending the FAC Clinic from 2011 to 2013 at Rigshospitalet, Denmark. A consultation included: risk assessment score sheet with items on infertility risk factors, anti-Müllerian hormone and ultrasound. The risk score was categorized as low, medium or high. After 2 years an email-based questionnaire was distributed regarding subsequent pregnancies. *Results.* The follow-up questionnaire was answered by 519 women (91.1%). The mean age was 35 years and 38% were single at inclusion. The majority (67.8%, 352/519) tried to conceive within 2 years after attending the FAC Clinic. At follow up, 73.6% (259/352) had achieved a pregnancy, 21% (74/352) were still trying and 5.4% (19/352) had given up. Two-thirds (65%) with only low risk scores conceived spontaneously within 12 months, although this figure was only 32% for women with at least one high risk score (n = 82). Accordingly, presence of at least one high risk score reduced the odds of achieving a pregnancy within 12 months by 75% (OR 0.25, 95% CI 0.12–0.52). *Conclusion.* The new FAC Clinic concept seems usable and offers a tool for fertility experts to guide women on how to fulfill their reproductive life-plan.

Abbreviations: AFC, antral follicle count; AMH, anti Müllerian hormone; AUC, area under the curve; FAC Clinic, Fertility Assessment and Counseling Clinic; TTP, time to pregnancy.

Introduction

Female reproduction is presently challenged and various pro-fertility concepts have been established to address this development (1,2). The notable changes in reproductive patterns within the past decades may be influenced by the increased female educational level and subsequently

Key Message

Fertility assessment and counseling can predict prolonged time to pregnancy and the concept can be used by fertility experts to guide women about their fertility status in order to fulfill their reproductive life-plan.

higher maternal age at first birth. In line with this, broader interpretations of "family planning," counseling opportunities and new treatments have emerged. Oocyte vitrification for nonmedical reasons and the option of single motherhood by donor insemination have been accepted as appropriate solutions in some parts of the world (3,4). The tendency to postpone family formation has resulted in decreased fertility rates, smaller families than desired and an increase in the demand for fertility treatment, especially in women >40 years of age (5). The aforementioned fertility issues and increasing awareness have introduced a demand for fertility screening (6,7).

The Fertility Assessment and Counseling Clinic (FAC Clinic) at Rigshospitalet in Copenhagen was initiated as an analogue to the "family planning clinics," that were introduced in the 1970s (8). The FAC clinic uses the same concept, based on self-referral, offering reproductive advice to women and men, but with a pro-fertility perspective. The purpose is to provide individual assessment of fertility risk factors and ovarian reserve to help women with no known history of infertility to fulfill their reproductive life-plan (1). The FAC Clinic is the first of its kind worldwide and a number of clinics based on the same concept have been initiated in four of the Nordic countries.

This study is the first to validate this new concept through a 2-year follow up after the initial consultation. The study aimed to analyze the predictive value of risk assessment in relation to time to pregnancy (TTP).

Material and Methods

The concept of the FAC Clinic has been described and discussed earlier (1). Briefly, the FAC Clinic was established in August 2011 as part of the ReproUnion collaborative study, co-financed by the European Union, Intereg V ÖKS. The clinic is open to men and women living in the Capital Region of Denmark or southern part of Sweden. No referral is needed, the consultations are free of charge, and appointments are booked by phone on a weekly basis. Couples who had already tried to conceive for more than a year in their present relationship at the time of booking, were informed to go elsewhere and seek direct medical assistance.

All women were examined by a fertility specialist. A consultation included: transvaginal ultrasound [antral follicle count (AFC), ovarian volume, pathology], full reproductive history and anti-Müllerian hormone (AMH) measurement. The women were informed of their potential risk factors and presumed ovarian reserve by a Risk Assessment Score Sheet (Figure 1) (1). The item scores were categorized as green/yellow (low risk), orange (medium risk) and red (high risk) for each risk factor.

Due to low numbers, the following risk factors were not included in the analyses regarding single predictors of TTP analyses, but were included in the validation of the overall risk assessment: ectopic pregnancies (n = 2), endometriosis (n = 10), myomas >3 cm in diameter (n = 6), abdominal fluid (n = 5), previous treatment with chemotherapy (n = 6), high stress level (n = 10), and previous ovarian or other lower abdominal operations (n = 13).

Initial study population at screening 2011–13 included the first 570 women attending the FAC Clinic from June 2011 to December 2013. All women completed a baseline web-based questionnaire before the consultation and an evaluation questionnaire immediately after the consultation.

The baseline questionnaire was partly based on the validated Swedish Fertility Awareness Questionnaire by Lampic et al. and a questionnaire from a previous Danish study from our group (9,10). The questionnaire included items regarding sociodemographic background, reproductive and medical history and lifestyle (smoking, alcohol and exercise) (see Supplementary material, Appendix S1).

Assessment of ovarian reserve parameters were estimated by AFC, ovarian volume and AMH. The number of antral follicles was counted and grouped into three predefined categories: 2–4, 5–7 and 8–10 mm. The ovarian volume was measured by the formula for a prolate ellipsoid using the longest longitudinal (d1), anteroposterior (d2), and transversal diameters (d3): volume = $(d1 \times d2 \times d3) \times \pi/6$ (11). All ultrasound scans were performed using the same equipment (BK pro focus ultrasound scanner, vaginal probe, transducer 4–9 MHz, BK Medical, Herlev, Denmark) and all examinations were carried out by the same team of five doctors throughout the period. At clinical examination, the investigator was unaware of the participants' questionnaire answers and their hormonal profile (AMH).

All blood samples were handled consistently: fresh samples were centrifuged approximately 1 h after sampling and serum was frozen at −24°C for a maximum of 14 days before being analyzed consecutively at the Department of Clinical Biochemistry, Rigshospitalet, Copenhagen using the Beckman Coulter enzyme immunometric assay, generation I (Immunotech Laboratories, Monrovia, CA, USA). The analytical sensitivity, and the intra-assay and inter-assay coefficients of variation were: 0.7 pmol/L, 12.3 and 14.2%, respectively (12).

Male partners were welcome to attend the clinic together with their female partners for assessment (sperm analysis, risk assessment score) (1), but only 28 in the present study did so. Sperm tests data were therefore not included in the statistical analyses.

The follow-up questionnaire was distributed by e-mail 2 years after the consultation. The primary data in the

Name:	**Personal ID:**

RISK FACTORS	**PARAMETER**	**LOW RISK**		**MEDIUM RISK**		**HIGH RISK**	
FEMALE AGE							
Age	Age (years)	Under 35		35–39		40 or above	
OVARIAN RESERVE AND CYCLE LENGTH							
Cycle length	Days	23 – 35		More than 35		Less than 23	
Antral follicle count (Sum of both ovaries)	N	11 – 30		5 – 10 or more than 30		Less than 5	
Anti-Müllerian hormone	pmol/L	10–50		5–9 or higher than 50		Lower than 5	
GYNECOLOGICAL HISTORY AND GENERAL HEALTH							
Months of trying to conceive	Months	Less than 6		6 – 12		Longer than 12	
Pelvic inflammatory disease	N	0		1-2		More than 3	
Ectopic pregnancy	N	0		1		2 or more	
Endometriosis	Yes/no	No		Yes		Endometriomas	
Pelvic surgery	Yes/no	No		Intestinal surgery		Surgery in ovaries/tubes	
Uterine fibroids (submucosal / intramural fibroids)	Major diameter	0		Less than 3 cm		More than 3 cm	
Intraperitoneal fluid/uterine malformation/hydrosalpinx	Yes/no	No				Yes	
Previous chemotherapy	Yes/no	No				Yes	
GENETIC DISPOSITIONS AND INTRAUTERINE EXPOSURE							
Maternal age at menopause	Age (years)	Above 50		45 – 50		Less than 45	
Mother smoked during pregnancy	Yes/no	No				Yes	
LIFESTYLE FACTORS							
BMI	kg/m^2	20 – 30		Lower than 20 or 30–35		More than 35	
Waist/hip ratio		Lower than 0.80		Higher than 0.80			
Smoking	Number per day	0		1–10		More than 10	
Alcohol	Drinks per week	0		1–6		More than 7	
Caffeinated beverage	Cups per day	Fewer than 6		More than 6			
Physical activity		Mild/ moderate		Excessive			
WORK ENVIRONMENT FACTORS							
Stress		None/ moderate		Highly			

Figure 1. Risk Assessment Score sheet used for structured risk evaluation of female clients attending the Fertility Assessment and Counseling Clinic at Rigshospitalet, Copenhagen University Hospital, Denmark. Reproduced from Hvidman HW, Petersen KB, Larsen EC, Macklon KT, Pinborg A, Nyboe Andersen A. Individual fertility assessment and pro-fertility counselling; should this be offered to women and men of reproductive age? Hum Reprod. 2015;30:9–15, with permission from Oxford Journals. [Color figure can be viewed at wileyonlinelibrary.com]

follow-up questionnaire were: changes in relationship status, pregnancies, pregnancy loss, deliveries, TTP, attempts to conceive and whether the women had undergone fertility treatment.

Population A was defined as women who had attempted a pregnancy within the 2 years of follow up after their visit to the FAC Clinic. Women reported the date(s) (day/month/year) within the 2 years at which the attempt(s) at pregnancy was initiated, and if relevant the date(s) at which pregnancy was achieved. Further, it was recorded whether the woman was still trying or had given up at the end of follow up. Only the time to a first pregnancy was used in the TTP analyses. Pregnancies were categorized as spontaneous or after fertility treatment. Single women who achieved a pregnancy with donor insemination were pooled with spontaneous pregnancies in the analyses. Population B was defined as the remaining women without any attempts to conceive within the 2 years of follow up.

Statistical analyses

Baseline characteristics were summarized as mean and standard deviation of continuous variables, or number and percentage of categorical variables. Continuous variables were compared with two-sample *t*-test and categorical variables with Pearson chi-square or Fisher's exact test. Descriptive statistics was made with the statistical software SPSS version 22 (IBM Corp., Armonk, NY, USA) and Microsoft Office Excel 2010 (Microsoft Corp., Redmond, WA, USA).

To evaluate the predictive potential of the risk factors from the risk assessment score sheet we performed univariate and multivariate logistic regression analyses for the outcome "spontaneous pregnancy within 12 months." Analyses included all women who started their attempt of pregnancy before, at the FAC consultation, or within the following year. Women who started their attempt of pregnancy later than 1 year after the FAC visit were excluded from analyses due to insufficient follow-up time. Women who were already attempting pregnancy when visiting the FAC Clinic were regarded as successful if pregnancy was achieved within 1 year of the consultation. It is important to note that the duration of pregnancy attempts before the consultation was included as an item in the risk assessment sheet and as a predictor in the statistical analyses. To further assess the predictive performance of the risk assessment we used internal validation methods (13). The predictive accuracy of the risk assessment expected at future consultations was estimated by the cross-validated area under the curve (AUC) using 10 000 bootstrap cross-validation steps (14,15).

To identify predictors of fertility treatment we performed univariate and multivariate competing risk regression for the cumulated incidence of women starting fertility treatment in which spontaneous pregnancy was considered a competing risk. Results from the similar analyses of cumulated incidence of spontaneous pregnancy were highly similar to those from the logistic regression analyses and results are therefore not shown.

Analyses were performed with R version 3.2.3 (https://www.r-project.org, Vienna, Austria), the rms package for logistic regression analyses and the timereg-package for competing risk analyses.

All participants gave written informed consent according to the Declaration of Helsinki for Medical Research involving Human Subjects. The establishment of a biobank was approved by the Scientific Ethical Committee of the Capital Region of Denmark (journal number: H-1-2011-081). Permission to store data was granted by the Data Protection Agency at Rigshospitalet (journal number: 30-0728).

Results

From June 2011 until December 2013 a total of 570 women attended the FAC Clinic. The response rate of the follow-up questionnaire was 91.1% (519/570). The present study therefore included 519 women of whom 352 (population A) had attempted to conceive and 167 (population B) had made no attempts to conceive within the 2 years following initial assessment. Among the 352 women in population A, 259 had conceived, 74 were currently trying to conceive and 19 had given up trying to conceive at follow up.

Demographic characteristics at initial consultation are shown in Table 1. Women in population A had a mean age of 35.4 ($\pm$ 4.4) years and most were in a heterosexual relationship at the time of the FAC Clinic consultation (70.1%), and at the time of follow up (80.1%). Furthermore, the women were well-educated and employed (Table 1).

Table 2 displays the distribution of fertility risk factors in population A (according to the risk assessment score sheet, Figure 1). As seen in Table 2, there was a significant difference in the age distribution ($p = 0.001$), cycle length ($p = 0.02$) and duration of unprotected intercourse ($p = 0.01$) between the three risk groups. The overall distributions of women with low, medium and high AFC and AMH risk scores were equal among the groups.

Table 2 also compares the distribution of other fertility risk factors. Significantly fewer had endometriosis ($p = 0.01$) or smoked ($p = 0.049$) among the women who conceived within the 2 years of follow up. No significant differences were detected among the remaining risk factors.

Family intentions at initial consultation are shown in Table 3, the women in population A and B did not differ in terms of previous pregnancies, deliveries, miscarriages

Table 1. Demographic characteristics of the women in populations A (n = 352) and B (n = 167).

	Population A	Population B	Total	p-values
Number	352	167	519	
Age at follow up, mean, SD	35.3 (4.3)	35.4 (4.6)	35.4 (4.4)	0.491[a]
Relationship status				
In a relationship at the FAC consultation, *n* (%)	248 (70.1)	71 (43.3)	319 (62.1)	0.001*[b]
In a relationship at the time of follow up, *n* (%)	282 (80.1)	80 (48.2)	362 (69.6)	0.001*[b]
Change of partner during the 2-year follow up, *n* (%)	48 (13.6)	31 (18.6)	79 (15.2)	0.141[b]
Highest completed education, *n* (%)				
None	0	1 (0.6)	1 (0.2)	0.134[c]
Lower secondary grade/10th grade	2 (0.6)	2 (1.3)	4 (0.8)	
High school degree/higher commercial examination/ higher technical examination	19 (5.5)	10 (6.3)	29 (5.8)	
Skilled education within trade, business, office etc.	20 (5.8)	10 (6.3)	30 (6.0)	
Short further education, less than 3 years	19 (5.5)	11 (6.9)	30 (6.0)	
Medium further education, 3–4 years	74 (21.6)	46 (28.7)	120 (23.9)	
Long further education, >4 years	195 (56.9)	70 (43.8)	265 (52.7)	
Other education	14 (4.1)	10 (6.3)	24 (4.8)	
Current job situation				
Working	273 (79.6)	115 (71.0)	388 (76.8)	0.029*[c]
Employment and training scheme	3 (0.9)	3 (1.9)	6 (1.2)	
Temporary leave of absence due to sickness	3 (0.9)	4 (2.5)	7 (1.4)	
Leave (pregnancy, unpaid)	0	2 (1.2)	2 (0.4)	
Unemployed	22 (6.4)	7 (4.3)	29 (5.7)	
Student/apprentice	37 (10.8)	25 (15.4)	62 (12.3)	
Registered unfit for work	0	1 (0.6)	1 (0.2)	
Other	5 (1.5)	3 (3.1)	10 (2.0)	
Household income				
Less than € 13 000	5 (1.5)	7 (4.3)	12 (2.4)	0.001*[b]
Between € 13 000 and € 27 000	23 (6.7)	26 (16.1)	49 (9.7)	
Between € 27 000 and € 40 000	40 (11.7)	23 (14.3)	63 (12.5)	
Between € 40 000 and € 54 000	68 (19.8)	35 (21.7)	103 (20.4)	
Between € 54 000 and € 80 000	85 (24.8)	44 (27.3)	129 (25.6)	
Between € 80 000 and € 107 000	109 (31.8)	21 (13.0)	130 (25.8)	
Between € 107 000 and € 134 000	11 (3.2)	2 (1.2)	13 (2.6)	
More than € 134 000	2 (0.6)	3 (1.9)	5 (1.0)	

Population A: women, who attempted to conceive within the 2 years of follow up.
Population B: women, who did not attempt to conceive within the 2 years of follow up.
[a]Mann–Whitney *U*-test.
[b]Pearson chi-squared test.
[c]Fisher's exact test.
*Significant $p < 0.05$.

and abortions. In both groups approximately one-fifth had conceived before (population A: 22.7 vs. population B: 21.6%, $p = 0.83$). There were significant differences between the two groups in relation to the desired number of children; 75% in population A wished for two or three children, whereas this was 60.5% in population B. Only 8.2% wished for just one child in population A, whereas this was 15% in population B ($p = 0.03$). Similarly, more women in population A had a pregnancy wish at the time of the consultation (A: 65.3 vs. B: 25.7%, $p < 0.001$) and follow up (A: 42.3 vs. B: 29.9%, $p < 0.001$). The women were asked whether they would bring forward the timing of pregnancy after consulting the FAC Clinic, to which 31% answered yes in population A compared with 22.8% in population B ($p < 0.001$). The most prevalent among the reasons for attending FAC listed by population A, was the wish for an assessment of their possibility to achieve a pregnancy (A: 53.4 vs. B: 62.9%, $p = 0.04$) (Table 3). Among population B it was knowledge of the possibility to postpone childbearing (B: 73.7 vs. A: 50.6%, $p = 0.001$).

With regards to pregnancies, attempts and fertility treatments at follow up we found a significantly lower mean age of the 259 women who achieved a pregnancy, compared with the 74 women who were still trying and the 19 women who had given up trying (34.9 vs. 36.2 vs. 38.1 years, $p = 0.002$). Similarly, there was a difference in relationship

Table 2. Risk assessment at the consultation at the Fertility Assessment and Counseling Clinic.

	Pregnant at follow up	Still trying at follow up	Given up trying at follow up	Total	*p*-values
Number	259	74	19	352	
Age, *n* (%)					
<35 years	163 (62.9)	35 (47.3)	6 (31.6)	204 (58.0)	0.001[a]*
35–39	83 (32.1)	32 (43.2)	8 (42.1)	123 (34.9)	
≥40	13 (5.0)	7 (9.5)	5 (26.3)	25 (7.1)	
Cycle length, days					
23–35	231 (89.2)	65 (87.8)	16 (84.2)	312 (88.7)	0.02[b]*
>35	24 (9.3)	3 (4.1)	3 (15.8)	30 (8.5)	
<23	4 (1.5)	6 (8.1)	0	10 (2.8)	
Antral follicle count, *n* (%)					
11–30	182 (70.3)	42 (56.8)	11 (57.9)	235 (90.7)	0.14[b]
5–10 or >30	69 (26.6)	30 (40.5)	8 (42.1)	107 (30.5)	
<5	8 (3.1)	2 (2.7)	0	10 (2.8)	
Anti-Müllerian hormone, pmol/L, *n* (%)					
10–50	176 (68.0)	54 (73.0)	10 (52.7)	240 (68.2)	0.36[b]
5–9 or >50	66 (25.5)	14 (18.9)	7 (36.8)	87 (24.7)	
<5	17 (6.5)	6 (8.1)	2 (10.5)	25 (7.1)	
Unprotected intercourse, *n* (%)					
Less than 6 months	186 (75.3)	59 (84.2)	9 (47.4)	254 (75.6)	0.01[b]*
6–12 months	46 (18.6)	8 (11.4)	5 (26.3)	59 (17.6)	
Longer than 12 months	15 (6.1)	3 (4.3)	5 (26.3)	23 (6.8)	
Previous pelvic inflammatory disease, including chlamydia, *n* (%)					
None	200 (77.5)	59 (79.7)	11 (61.1)	270 (77.1)	0.19[b]
1–2 infections	56 (21.7)	13 (17.6)	7 (39.9)	76 (21.7)	
3 or more infections	2 (0.8)	2 (2.7)	0	4 (1.2)	
Diagnosed with endometriosis, *n* (%)					
No	254 (98.1)	70 (94.6)	17 (89.5)	341 (97.2)	0.01[b]*
Yes: unspecific	1 (0.4)	4 (5.4)	2 (10.5)	7 (2.0)	
Yes: endometrial cyst(s) in the ovaries	3 (1.2)	0	0	3 (0.8)	
Previous pelvic surgery, *n* (%)					
No	224 (88.2)	67 (90.5)	13 (72.2)	304 (87.9)	0.06[b]
Yes: on the intestines (appendicitis)	23 (9.1)	4 (5.4)	2 (11.1)	29 (8.4)	
Yes: on the tubae or the ovaries	7 (2.8)	3 (4.1)	3 (16.7)	13 (3.7)	
Myoma in the uterus, *n* (%)					
No	208 (95.8)	60 (92.3)	13 (86.6)	281 (94.6)	0.18[b]
Yes: <3 cm in diameter	6 (2.8)	3 (4.6)	1 (6.7)	10 (3.4)	
Yes: ≥3 cm in diameter	3 (1.4)	2 (3.1)	1 (6.7)	6 (2.0)	
Abdominal fluid, *n* (%)					
No	211 (98.1)	64 (98.5)	15 (100)	290 (98.3)	0.99[b]
Yes	4 (1.9)	1 (1.5)	0	5 (1.7)	
Previous chemotherapy, *n* (%)					
No	250 (98.4)	73 (98.6)	18 (94.7)	341 (98.3)	0.30[b]
Yes	4 (1.6)	1 (1.4)	1 (5.3)	6 (1.7)	
Maternal age at menopause, years, *n* (%)					
<45	13 (5.0)	7 (9.5)	0	20 (5.7)	0.55[b]
45–50	84 (32.4)	22 (29.7)	6 (31.6)	112 (31.8)	
>50	115 (44.4)	29 (39.2)	8 (42.1)	152 (43.2)	
Don't know	37 (14.2)	16 (21.6)	5 (26.3)	68 (19.3)	
Prenatal exposure to maternal smoking, *n* (%)					
Yes	85 (32.9)	18 (24.3)	6 (31.6)	109 (31.0)	0.49[b]
No	155 (59.8)	52 (70.3)	11 (57.9)	218 (61.9)	
Don't know	19 (7.3)	4 (5.4)	2 (10.5)	25 (7.1)	

Table 2. Continued

	Pregnant at follow up	Still trying at follow up	Given up trying at follow up	Total	*p*-values
BMI (kg/m^2), *n* (%)					
20–35	209 (81.0)	52 (70.3)	15 (78.9)	276 (78.6)	0.27[b]
<20 or 30–35	46 (17.8)	20 (27.0)	4 (21.1)	70 (19.9)	
>35	3 (1.2)	2 (2.7)	0	5 (1.5)	
Waist:hip ratio, *n* (%)					
≤0.8	167 (65.0)	44 (60.3)	9 (52.9)	220 (63.4)	0.48[b]
>0.8	90 (35.0)	29 (39.7)	8 (47.1)	127 (36.6)	
Cigarettes per day, *n* (%)					
None, not daily	222 (85.7)	62 (83.8)	12 (63.2)	296 (84.3)	0.049[b]*
1–10 cigarettes	27 (10.5)	7 (9.5)	6 (31.6)	40 (11.4)	
>10 cigarettes	9 (3.5)	5 (6.8)	1 (5.3)	15 (4.3)	
Alcohol per week, *n* (%)					
None	58 (22.6)	15 (20.3)	4 (21.1)	77 (22.0)	0.80[b]
1–6 units	168 (65.4)	49 (66.2)	11 (57.9)	228 (65.1)	
7 or more units	31 (12.0)	10 (13.5)	4 (21.0)	45 (12.9)	
Cups of coffee per day, *n* (%)					
Fewer than six	246 (95.3)	71 (95.9)	19 (100)	336 (95.7)	0.99[b]
Six or more	12 (4.7)	3 (4.1)	0	15 (4.3)	
Exercise per week, *n* (%)					
Minimum/moderate	233 (92.8)	70 (95.9)	19 (100)	322 (93.9)	0.50[b]
Excessive training	18 (7.2)	3 (4.1)	0	21 (6.1)	
Self reported stress level, *n* (%)					
None/moderate	246 (97.2)	70 (95.9)	19 (100)	335 (97.1)	0.83[b]
Highly	7 (2.8)	3 (4.1)	0	10 (2.9)	

Population A: women, who attempted to conceive within the 2 years of follow up.
Population B: women, who did not attempt to conceive within the 2 years of follow up.
[a]Pearson chi-squared test.
[b]Fisher's exact test.
*Significant $p < 0.05$.

status at follow up with a higher proportion of women in a heterosexual relationship among the women, who conceived within 2 years (83.0 vs. 75.7 vs. 57.9%, $p = 0.01$).

More than half of the pregnancies were spontaneous and planned (142/259; 54.8%). Almost one-third of the pregnancies (83/259; 32%) were achieved by fertility treatment. Among the 83 women who received fertility treatment, intrauterine insemination with husband's semen was the most frequently used procedure among the 49 couples (20/49; 40.8%), and intrauterine insemination with donor semen among the 34 single women (19/34; 55.9%). Of the 259 pregnancies, 161 (62.2%) resulted in a liveborn child and 50 women (19.3%) were still pregnant at the time of the 2-year follow up. Twelve women had an induced abortion (4.6%) and 34 women had a spontaneous miscarriage (13.1%).

The majority of women, who were still trying to conceive, had received fertility treatment at the time of follow up (40/74; 54.1%). This figure was 26.3% for the women who had given up trying.

The results of the single factor and multiple logistic regression analyses of the chance of spontaneous pregnancy within 12 months are displayed in Table 4. A total of 320 women attempted pregnancy starting at the time of the FAC consultation, before or within 1 year after the consultation. Only three women (1.2%) had entirely green scores. For this reason they were pooled with the women with one yellow score and analyzed as low risk. Figure 2 shows the cumulative incidence curves of spontaneous pregnancies in relation to the risk assessment. Two-thirds of the women with only low risk scores (green/yellow) (33/51; 64.7%) conceived spontaneously within 12 months, whereas this figure was 101/194 (52.1%) among the women with at least one medium score (orange) and only 25/75 (32.5%) for women with at least one high risk score (red). Accordingly, the presence of at least one high risk score (red) reduced the odds of achieving pregnancy within 12 months by 75% (OR 0.25, 95% CI 0.12–0.52, $p < 0.001$) compared with women with only green and yellow scores (Table 3). Similarly, the presence of at least one medium risk score (orange) reduced the odds for a spontaneous pregnancy by 47%, although this was only a tendency (OR 0.53, 95% CI 0.28–0.98).

Table 3. Personal considerations in relation to childbearing and reason for attending the Fertility Assessment and Counseling Clinic.

	Cohort	Controls	Total	*p*-values
Number	Population A	Population B	519	
Previous pregnancies, *n* (%)				
Yes	80 (22.7)	36 (21.6)	116 (22.4)	0.827[c]
None	266 (75.6)	127 (76.0)	393 (75.7)	
Don't know	6 (1.7)	4 (2.4)	10 (1.9)	
Previous reproductive history, *n* (%)				
Delivery of a live born child	17 (20.7)	6 (15.8)	23 (19.2)	0.204[c]
Spontaneous abortion	16 (19.5)	5 (13.2)	21 (17.5)	
Induced abortion	48 (58.5)	25 (65.8)	73 (60.8)	
Stillbirth	0	2 (5.3)	2 (1.7)	
Wish for number of children, *n* (%)				
1	29 (8.2)	25 (15.0)	54 (10.4)	0.026*[b]
2	192 (54.5)	81 (48.5)	273 (52.6)	
3	72 (20.5)	20 (12.0)	92 (17.7)	
4	7 (2.0)	2 (1.2)	9 (1.7)	
5	1 (0.3)	0	1 (0.2)	
Don't know	51 (14.5)	39 (23.4)	90 (17.3)	
Wish for number of children, mean (SD)	2.2 (0.65)	2.0 (0.65)	2.14 (0.66)	0.002*[a]
Pregnancy wish, *n* (%)				
Pregnancy wish at the time of consultation	230 (65.3)	43 (25.7)	273 (52.6)	0.001*[b]
Pregnancy wish at the time of follow up	149 (42.3)	50 (29.9)	199 (38.3)	0.001*[b]
Would you bring forward the timing of pregnancy after FACC?				
Yes: definitely	37 (10.5)	3 (1.8)	40 (7.7)	0.001*[b]
Yes: most likely	72 (20.5)	35 (21.0)	107 (20.6)	
I don't know	169 (48.0)	75 (44.9)	244 (47.0)	
No: probably not	55 (15.6)	47 (28.1)	102 (19.7)	
No: definitely not	19 (5.4)	7 (4.2)	26 (5.0)	
Main reason for attending the FACC, *n* (%)				
How long can I postpone childbearing	178 (50.6)	123 (73.7)	301 (58.0)	0.001*[b]
Check: because it was possible	188 (53.4)	105 (62.9)	293 (56.5)	0.042*[b]
Worried about my fecundity	179 (50.9)	89 (53.3)	268 (51.6)	0.603[b]
Knowledge: how to optimize my chances	120 (34.1)	59 (35.3)	179 (34.5)	0.782[b]
Currently trying to get pregnant	127 (36.1)	7 (4.2)	134 (25.8)	0.001*[b]
Due to a doctor's recommendation	10 (2.8)	5 (3.0)	15 (2.9)	0.560[c]
My partner wanted me to attend the consultation	9 (2.6)	0	9 (1.7)	0.029*[c]

FACC, Fertility Assessment and Counseling Clinic.
p-values indicate the difference between the cohort and reference group.
[a]Mann–Whitney *U*-test.
[b]Pearson chi-squared test.
[c]Fischer's exact test.
*Significant $p < 0.05$.

Predictive performance of risk factors and cross-validated AUCs are shown in Table 4. The best single predictors of spontaneous pregnancy within 12 months were age (AUC = 0.569), followed by unprotected intercourse (AUC = 0.545), and hip:waist ratio (AUC = 0.541). Many of the risk factors only had a slight predictive performance including BMI, alcohol and coffee consumption. The FAC risk assessment score provided the best overall predictive performance (AUC = 0.606), whereas the multivariate logistic regression model including all risk factors had a slightly inferior predictive performance (AUC = 0.574).

Within the 2 years of follow up, 128 women received fertility treatment. In the competing risk regression, the presence of at least one red (high) risk score displayed an increased hazard ratio of 4.5 (95% CI 1.1–29.7) for fertility treatment. None of the remaining predictors was associated with a significantly increased incidence of needing fertility treatment in the analyses (data not shown).

Discussion

This is the first prospective study to validate an individual fertility assessment and counseling concept. Our results

Table 4. Univariate and multivariate regression analyses of risk factors and area under the curve in relation to the chance of a time to pregnancy <12 months.

	Univariate[a]			Multivariate[b]			
	OR	95% CI	*p*-values	OR	95% CI	*p*-values	AUC[c]
Risk assessment score							
Low: Green/yellow (categorical)	Ref.		0.00063*				0.606
Medium: Orange	0.53	0.28–0.98					
High: Red	0.25	0.12–0.52					
Age, years							
<35 (categorical)	Ref.		0.017*	Reference		0.70	0.569
35–39	0.65	0.40–1.04		0.82	0.42–1.61		
≥40	0.30	0.11–0.77		0.60	0.15–2.32		
Cycle length, days							
23–35 (categorical)	Ref.		0.07	Ref.		0.12	0.532
>35	0.52	0.22–1.20		0.59	0.21–1.62		
<23	0.27	0.04–1.12		0.16	0.01–1.14		
Antral follicle count							
11–30 (categorical)	Ref.		0.23	Ref.		0.60	0.539
>30	0.67	0.31–1.41		0.72	0.25–2.04		
5–10	0.63	0.36–1.10		0.60	0.25–1.38		
<5	0.43	0.09–1.7		0.52	0.07–3.57		
Anti-Müllerian hormone, pmol/L							
10–50 (categorical)	Ref.		0.89	Ref.		0.98	0.499
>50	0.81	0.43–1.51		1.11	0.46–2.75		
5–9	0.84	0.39–1.80		1.14	0.39–3.38		
<5	0.88	0.37–2.08		1.29	0.36–4.78		
Unprotected intercourse							
Less than 6 months (categorical)	Ref.		0.08	Ref.		0.15	0.545
6–12 months	0.61	0.33–1.11		0.48	0.22–1.02		
Longer than 12 months	0.45	0.17–1.12		0.75	0.23–2.34		
Previous pelvic inflammatory disease, including Chlamydia							
None (categorical)	Ref.		0.83	Ref.		0.91	0.501
1–2 infections	1.18	0.69–2.01		0.92	0.46–1.83		
3 or more infections	1.05	0.12–8.87		0.67	0.08–6.02		
Maternal age at menopause, years							
>50 (categorical)	Ref.		0.73	Ref.		0.92	0.501
45–50	1.12	0.67–1.88		1.06	0.58–1.94		
<45	0.77	0.29–1.98		0.84	0.3–2.41		
Prenatal exposure to maternal smoking							
No (categorical)	Ref.		0.048*	Ref.		0.58	0.538
Yes	1.23	0.76–2.00		1.07	0.58–1.97		
Don't know	0.34	0.11–0.91		0.39	0.05–2.42		
BMI (kg/m^2)							
20–35 (categorical)	Ref.		0.47	Ref.		0.41	0.519
<20	0.70	0.39–1.26		0.61	0.28–1.32		
30–35	0.75	0.18–2.90		1.41	0.22–972		
>35	0.31	0.02–2.48		0.28	0.01–2.53		
Hip:waist ratio							
≤0.8 (categorical)	Ref.		0.086	Ref.		0.39	0.541
>0.8	0.67	0.42–1.06		0.77	0.43–1.40		
Cigarettes per day							
None, not daily (categorical)	Ref.		0.78	Ref.		0.68	0.501
1–10 cigarettes	0.79	0.39–1.58		0.77	0.34–1.75		
>10 cigarettes	0.86	0.30–2.47		1.49	0.34–7.11		

Table 4. Continued

	Univariate[a]			Multivariate[b]			
	OR	95% CI	*p*-values	OR	95% CI	*p*-values	AUC[c]
Alcohol per week							
None (categorical)	Ref.		0.52	Ref.		0.30	0.514
1–6 units	1.36	0.79–2.35		1.15	0.58–2.25		
7 or more units	1.13	0.51–2.51		0.55	0.18–1.58		
Cups of coffee per day							
Fewer than six (categorical)	Ref.		0.29	Ref.		0.10	0.507
Six or more	0.55	0.17–1.64		0.30	0.06–1.26		
Exercise per week							
Minimum/moderate (categorical)	Ref.		0.31	Ref.		0.21	0.508
Excessive training	1.61	0.65–4.21		2.17	0.66–8.39		

Categorical: calculated as a categorical variable.
[a]Univariate analyses: not adjusted.
[b]Multivariate analyses: adjusted for all other risk factors.
[c]AUC, area under the curve using 10 000 bootstrap cross-validation steps.
*Significant $p < 0.05$.

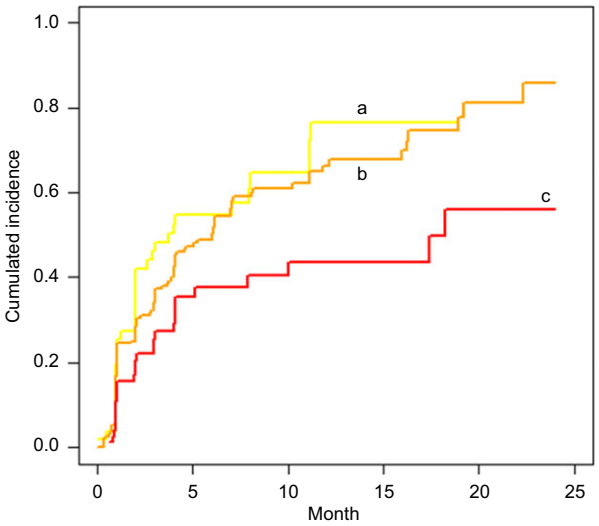

Figure 2. Cumulated incidence of spontaneous pregnancies grouped by Fertility Assessment and Counseling Clinic risk score. The figure displays the cumulated incidences of spontaneous pregnancies over 24 months of follow up for women in population A grouped according to the estimated score after a consultation at the Fertility Assessment and Counseling Clinic.
[a]Yellow, low risk score.
[b]Orange, medium risk score.
[c]Red, high risk score. [Color figure can be viewed at wileyonlinelibrary.com]

show a predictive value of the risk assessment score, as the odds of achieving a pregnancy within 12 months was decreased by 75% with the presence of just one high risk score, and by 41% with the presence of one or more orange scores. Furthermore, the cumulated incidence of women receiving fertility treatment was increased among the women with a high risk score corresponding to a hazard ratio of 4.5. Despite a mean age of 35 years, half of the women conceived within the 2 years of follow up, but one-third of these pregnancies were achieved by medically assisted reproduction.

The construction of the risk assessment score sheet was based on the available literature in 2011 regarding known or suspected fertility risk factors, and recommendations from the Danish Health authority (1). The age-related decrease in women's fecundity is well-known (16,17), as well as the correlation between cycle length variability in the perimenopausal period (18), and the risk of prolonged TTP due to previous chlamydia infections and subsequent tubal factor infertility (19).

Whether a low AFC or AMH is associated with TTP in spontaneously achieved conceptions remains controversial. A recent prospective American study of 1202 women with one or two pregnancy losses did not find a correlation between AMH and TTP (20). The authors of a Swiss observational study of 87 women with spontaneous pregnancies concluded that only age, and not AMH, as a continuous variable, was related to TTP, which is in line with the findings of this study (21). A Danish study of 186 young women in their mid-20s found an association of prolonged TTP in women with a high AMH, but no impact if the AMH was low (22). In contrast, an American study of 98 women in their 30s found AMH to be a predictor of age-related reductions in fecundity (23). We would still advocate for the use of AMH in a FAC setting. First, AMH is a proxy for the number of primordial follicles and hence the ovarian reserve. AMH decreases with ovarian aging and provides useful information when predicting imminent premature ovarian insufficiency and menopause (24,25). Second, several studies have found

AMH to be related to outcome response to ovarian stimulation in terms of number of oocytes retrieved and to some extent the chance of a livebirth, which is relevant for the women with partners found to have very low sperm quality at the consultation (26), as they may need assisted reproductive technology. Lastly, AMH in combination with AFC is the best available option so far for estimating the ovarian reserve in relation to biological age compared with chronological age (27). It remains a possibility that the long-term prognosis for accomplishing the desired family size may be related to AMH and AFC levels, but this has to be substantiated.

Women and men request full programming of reproduction ranging from contraception to pro-fertility behavior to ensure that they can achieve the desired family size (6,7,28). As discussed earlier by our group, false-positive findings of having low fertility chances when estimating the ovarian reserve may cause unnecessary anxiety, neglect of contraception and premature fertility treatment (1). False-positive findings could be very low AMH and AFC caused by oral contraceptive use or assay problems (12,29). Individuals are not given a specific prognosis, but an estimate of their reproductive potential and, as shown earlier, the risk assessment score is useful in identifying those at risk of prolonged TTP. The decision of childbearing shortly after the consultation at the FAC Clinic is presumably not solely related to the information on the individual ovarian reserve. This correlates with previous findings on factors influencing women's decisions about timing of motherhood. Benzies et al. performed a qualitative study on 45 Canadian women aged 20–48 years and found independence, stable relationships and declining fertility to be the primary factors for timing motherhood (30). Similarly, a cross-sectional study from our institution of 863 healthcare workers aged 20–40 years listed the most important prerequisites as: a stable relationship, completion of one's studies, a sound financial situation, a job that can be combined with children, access to public day care and the possibility of travelling (31). Nonetheless, the answers will evidently influence the considerations and subsequent actions regarding family planning. Other initiatives have been examined to increase women's and men's knowledge on fertility. Daniluk and Koert studied the educational efficacy of a fertility awareness website. They found significantly increased knowledge scores after the web-based intervention, but after 6 months of follow up there was a tendency to return to pre-intervention levels (32). Two recent randomized controlled trials, with the aims of individual Reproductive Life Planning in relation to contraceptive counseling and tailored education of fertility awareness, showed a significantly increased knowledge of reproduction in the intervention groups (28,33), Therefore, counseling on the individual level and being aware of the results provided with this study may increase the impact and counseling could influence the timing of pregnancy for future clients attending the FAC Clinic.

The FAC Clinic was partly initiated to inform men and women of their reproductive potential with the aim of reducing the need for fertility treatments. Hence, it was unexpected that almost one-third of the pregnancies in the 2-year follow up were achieved by medically assisted reproduction. There could be several reasons for this. First, the women's mean age of 35 years, as increased female age increases the need for fertility treatment due to accumulation of reproductive threats (endometriosis, chlamydia, myomas) (34); second, selection bias, as women may attend the FAC Clinic because they are concerned about their fecundity which could be due to previous unprotected intercourse without pregnancies, anovulation, or impaired sperm quality; third, Danish single women in their mid to late thirties have the opportunity to become solo-mothers by donor insemination (3,35); and lastly, reduced sperm quality among Danish men as shown in a study of 4867 men with a median age of 19 years in whom optimal semen quality was found in only 23%. Additionally, one-fourth were expected to experience prolonged waiting TTP and another 15% were at risk of the need of fertility treatment (36).

The women attending the FAC Clinic were well-educated and employed. The women were concerned about their ovarian reserve and reproductive time-span, which could imply potential selection bias. The homogeneity of the included women and the relatively short follow-up period may impede the predictive value of the continuous variables in the risk assessment. Hence, we decided not to revise the risk assessment score sheet until further research, including a 5-year follow up, has been completed. Inclusion of more clients may allow further analyses of more extreme findings in terms of for instance advanced age, very low ovarian reserve and extreme health behavior. Another main limitation is the missing information of the partner's sperm quality. Yet, it has to be noted that the diagnostic accuracy and predictive value of only one semen analysis in relation to TTP is limited (37). Furthermore, no data on coitus frequency were available, which could likewise have an influence on the results.

The follow-up questionnaire was based on retrospective data, which could induce recall bias and impair TTP analyses, as the data are self-reported and unverifiable by medical records (38). Nevertheless, a previous study of 1647 women with a much longer follow-up period found high accuracy of the reported TTP data (39).

With reference to the validity of the measurements of AMH, a recent review stated that fluctuations of AMH in the menstrual cycle appear to be random and minor, so

permitting AMH measurement independently of the cycle phase (27). Nonetheless, AMH is influenced by other factors such as oral contraceptive use (12,29). The statistical analyses were not adjusted for this, as the risk assessment score sheet did not include this parameter. Oral contraception use is recorded at the consultation and the impact has previously been described in an earlier paper by our group (29).

Conclusions

The FAC Clinic was initiated to provide women with information on their current fertility status to prevent involuntary childlessness, infertility and smaller families than desired. The risk assessment does allow prediction of the time to natural conceptions but does not seem able to prevent the need for fertility treatment in many cases. The FAC concept should instead be considered as a useful tool for fertility experts to counsel women and men on how to fulfill their reproductive life plan, including advice on when to proceed to medically assisted reproduction.

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References

1. Hvidman HW, Petersen KB, Larsen EC, Macklon KT, Pinborg A, Nyboe Andersen A. Individual fertility assessment and pro-fertility counselling; should this be offered to women and men of reproductive age? Hum Reprod. 2015;30:9–15.
2. Bunting L, Boivin J. Development and preliminary validation of the fertility status awareness tool: FertiSTAT. Hum Reprod. 2010;25:1722–33.
3. Salomon M, Sylvest R, Hansson H, Nyboe Andersen A, Schmidt L. Sociodemographic characteristics and attitudes towards motherhood among single women compared with cohabiting women treated with donor semen – a Danish multicenter study. Acta Obstet Gynecol Scand. 2015;94:473–81.
4. Zadeh S, Freeman T, Golombok S. Absence or presence? Complexities in the donor narratives of single mothers using sperm donation. Hum Reprod. 2016;31:117–24.
5. Leridon H, Slama R. The impact of a decline in fecundity and of pregnancy postponement on final number of children and demand for assisted reproduction technology. Hum Reprod. 2008;23:1312–9.
6. Seifer DB, Minkoff H, Merhi Z. Putting 'family' back in family planning. Hum Reprod. 2015;30:16–9.
7. Kushnir VA, Barad DH, Gleicher N. Ovarian reserve screening before contraception? Reprod Biomed Online. 2014;29:527–9.
8. Jaffe FS. Fertility control policy, social policy and population policy in an industrialized country. Fam Plann Perspect. 1974;6:164–9.
9. Bentzen JG, Forman JL, Larsen EC, Pinborg A, Johannsen TH, Schmidt L, et al. Maternal menopause as a predictor of anti-Mullerian hormone level and antral follicle count in daughters during reproductive age. Hum Reprod. 2013;28:247–55.
10. Lampic C, Svanberg AS, Karlstrom P, Tyden T. Fertility awareness, intentions concerning childbearing, and attitudes towards parenthood among female and male academics. Hum Reprod. 2006;21:558–64.
11. Rosendahl M, Ernst E, Rasmussen PE, Andersen CY. True ovarian volume is underestimated by two-dimensional transvaginal ultrasound measurement. Fertil Steril. 2010;93:995–8.
12. Bentzen JG, Forman JL, Pinborg A, Lidegaard O, Larsen EC, Friis-Hansen L, et al. Ovarian reserve parameters: a comparison between users and non-users of hormonal contraception. Reprod Biomed Online. 2012;25:612–9.
13. Steyerberg EW, Harrell FE Jr, Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. J Clin Epidemiol. 2001;54:774–81.
14. Efron B, Tibshirani R. Improvements on cross-validation: the .632+ bootstrap method. J Am Stat Assoc. 1997;92:548–60.
15. Gerds TA, Cai T, Schumacher M. The performance of risk prediction models. Biom J. 2008;50:457–79.
16. Larsen U, Yan S. The age pattern of fecundability: an analysis of French Canadian and Hutterite birth histories. Soc Biol. 2000;47:34–50.
17. Leridon H. Can assisted reproduction technology compensate for the natural decline in fertility with age? A model assessment Hum Reprod. 2004;19:1548–53.
18. O'Connor KA, Holman DJ, Wood JW. Menstrual cycle variability and the perimenopause. Am J Hum Biol. 2001;13:465–78.
19. Land JA, Van Bergen JE, Morre SA, Postma MJ. Epidemiology of *Chlamydia trachomatis* infection in women and the cost-effectiveness of screening. Hum Reprod Update. 2010;16:189–204.

20. Zarek SM, Mitchell EM, Sjaarda LA, Mumford SL, Silver RM, Stanford JB, et al. Is anti-Mullerian hormone associated with fecundability? Findings from the EAGeR Trial. J Clin Endocrinol Metab. 2015;100:4215–21.
21. Streuli I, de Mouzon J, Paccolat C, Chapron C, Petignat P, Irion OP, et al. AMH concentration is not related to effective time to pregnancy in women who conceive naturally. Reprod Biomed Online. 2014;28:216–24.
22. Hagen CP, Vestergaard S, Juul A, Skakkebaek NE, Andersson AM, Main KM, et al. Low concentration of circulating antimullerian hormone is not predictive of reduced fecundability in young healthy women: a prospective cohort study. Fertil Steril. 2012;98:1602–8.e2.
23. Steiner AZ, Herring AH, Kesner JS, Meadows JW, Stanczyk FZ, Hoberman S, et al. Antimullerian hormone as a predictor of natural fecundability in women aged 30–42 years. Obstet Gynecol. 2011;117:798–804.
24. Nelson SM, Telfer EE, Anderson RA. The ageing ovary and uterus: new biological insights. Hum Reprod Update. 2013;19:67–83.
25. Broer SL, Eijkemans MJ, Scheffer GJ, van Rooij IA, de Vet A, Themmen AP, et al. Anti-mullerian hormone predicts menopause: a long-term follow-up study in normoovulatory women. J Clin Endocrinol Metab. 2011;96:2532–9.
26. Tal R, Tal O, Seifer BJ, Seifer DB. Antimullerian hormone as predictor of implantation and clinical pregnancy after assisted conception: a systematic review and meta-analysis. Fertil Steril. 2015;103:119–30.e3.
27. Dewailly D, Andersen CY, Balen A, Broekmans F, Dilaver N, Fanchin R, et al. The physiology and clinical utility of anti-Mullerian hormone in women. Hum Reprod Update. 2014;20:370–85.
28. Stern J, Larsson M, Kristiansson P, Tyden T. Introducing reproductive life plan-based information in contraceptive counselling: an RCT. Hum Reprod. 2013;28:2450–61.
29. Birch Petersen K, Hvidman HW, Forman JL, Pinborg A, Larsen EC, Macklon KT, et al. Ovarian reserve assessment in users of oral contraception seeking fertility advice on their reproductive lifespan. Hum Reprod. 2015;30:2364–75.
30. Benzies K, Tough S, Tofflemire K, Frick C, Faber A, Newburn-Cook C. Factors influencing women's decisions about timing of motherhood. J Obstet Gynecol Neonatal Nurs. 2006;35:625–33.
31. Mortensen LL, Hegaard HK, Andersen AN, Bentzen JG. Attitudes towards motherhood and fertility awareness among 20–40-year-old female healthcare professionals. Eur J Contracept Reprod Health Care. 2012;17:468–81.
32. Daniluk JC, Koert E. Fertility awareness online: the efficacy of a fertility education website in increasing knowledge and changing fertility beliefs. Hum Reprod. 2015;30:353–63.
33. Garcia D, Vassena R, Prat A, Vernaeve V. Increasing fertility knowledge and awareness by tailored education: a randomized controlled trial. Reprod Biomed Online. 2016;32:113–20.
34. Liu K, Case A. Advanced reproductive age and fertility. J Obstet Gynaecol Can. 2011;33:1165–75.
35. Birch Petersen K, Hvidman HW, Sylvest R, Pinborg A, Larsen EC, Macklon KT, et al. Family intentions and personal considerations on postponing childbearing in childless cohabiting and single women aged 35–43 seeking fertility assessment and counselling. Hum Reprod. 2015;30:2563–74.
36. Jorgensen N, Joensen UN, Jensen TK, Jensen MB, Almstrup K, Olesen IA, et al. Human semen quality in the new millennium: a prospective cross-sectional population-based study of 4867 men. BMJ Open. 2012;2:e000990.
37. Buck Louis GM, Sundaram R, Schisterman EF, Sweeney A, Lynch CD, Kim S, et al. Semen quality and time to pregnancy: the Longitudinal Investigation of Fertility and the Environment Study. Fertil Steril. 2014;101:453–62.
38. Baird DD, Steiner AZ. Anti-Mullerian hormone: a potential new tool in epidemiologic studies of female fecundability. Am J Epidemiol. 2012;175:245–9.
39. Joffe M, Villard L, Li Z, Plowman R, Vessey M. A time to pregnancy questionnaire designed for long term recall: validity in Oxford, England. J Epidemiol Community Health. 1995;49:314–9.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Fertility Assessment and Counseling Clinic. Initial questionnaire before the consultation.