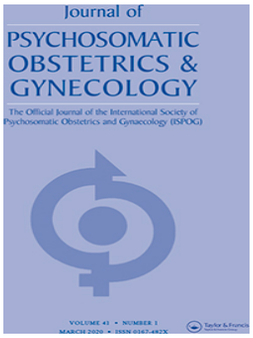

Journal of Psychosomatic Obstetrics & Gynecology

ISSN: 0167-482X (Print) 1743-8942 (Online) Journal homepage: https://www.tandfonline.com/loi/ipob20

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To cite this article: Yvonne O'Brien, Caroline Kelleher & Mary Wingfield (2020) "So what happens next?" exploring the psychological and emotional impact of anti-Mullerian hormone testing, Journal of Psychosomatic Obstetrics & Gynecology, 41:1, 30-37, DOI: 10.1080/0167482X.2018.1541980

To link to this article: https://doi.org/10.1080/0167482X.2018.1541980

JOURNAL OF PSYCHOSOMATIC OBSTETRICS & GYNECOLOGY
2020, VOL. 41, NO. 1, 30–37
https://doi.org/10.1080/0167482X.2018.1541980

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ORIGINAL ARTICLE

"So what happens next?" exploring the psychological and emotional impact of anti-Mullerian hormone testing

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ABSTRACT

Research Question: Significant medical benefits could be derived from universal AMH screening for women in their mid to late twenties. We aimed to investigate the psychological and emotional responses of women to being informed of their anti-Mullerian hormone (AMH) result with a view to informing the possible introduction of universal AMH screening.

Materials and methods: This was a prospective qualitative study using semi-structured in-depth interviews of women attending a reproductive medicine clinic who had ovarian reserve testing performed via measurement of serum AMH levels, as part of their gynecological investigations. A semistructured interview schedule was developed after a review of the literature. A purposive sample of women was recruited, and data collection continued until thematic saturation was reached ($n = 10$). The number of women interviewed is low as this was a pilot qualitative study of a two-part study. The next part of the study involves the development of a quantitative questionnaire related to the key themes identified in this study to be based on a much larger group of women. Interviews were audiotaped, transcribed verbatim and imported into QSR NVivo pro 11 for analysis.

Results: Three key themes emerged from the data: the experience of AMH testing, the response to the AMH result, and suggested lessons for medical professionals. The theme of the experience of AMH testing describes and reflects two sub-themes: the reasons for ovarian reserve testing and the potential barriers that may prevent women from accessing testing. A further key focus of this study was the emotional and psychological responses to receiving an AMH result and this emerged as a major theme in the interviews. Women described the significant impact that their individual result had on a number of lifestyle and behavioral factors and how it impacted on their gender identity. Lessons for medical professionals including the appreciation of the patient's awareness of the test and how the test result was relayed to the patient were important factors in how they dealt with the result. There were mixed reactions and opinions from the group in relation to the introduction of AMH testing as a screening tool for all young women.

Conclusions: Knowledge and communication of a low AMH result has a negative psychological impact. The findings from this study support the move to further explore the psychological and emotional impact of the test with the development of a quantitative questionnaire.

ARTICLE HISTORY
Received 30 April 2018
Revised 17 September 2018
Accepted 25 October 2018

KEYWORDS
Fertility; qualitative methods; reproductive medicine; infertility; women's health

Key message

Significant psychological stress can be associated with receiving an AMH result and further research is needed before this introduced as a screening tool.

Introduction

In the last four decades, increasing numbers of women are postponing childbirth [1]. Ireland is no exception – the average age of women giving birth rose from 30.8 years in 2004 to 32.1 years in 2013 [2]. Parental readiness, relationship status and attainment of career and educational pursuits are influencing this trend [3].

Ovarian reserve (OR) is a term widely used to reflect a woman's current supply of oocytes and is closely related with reproductive potential and reproductive lifespan [4]. The quantitative level of ovarian reserve can have a significant effect on a woman's future reproductive potential and on success rates with assisted reproduction [5,6]. AMH has been used to good effect as a useful predictor of the response of the ovary to controlled ovarian stimulation (COS) in ART treatment [7]. However, there are other studies that show that AMH testing does not predict success in immediate natural conception [8–10]. Nevertheless, all these studies point toward AMH as a very good quantitative marker of ovarian reserve and, consequently, response to stimulation.

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It can vary markedly between individuals due to natural atretic loss, or as a result of treatments that may have hastened follicle depletion. Best practice markers of ovarian reserve assessment include serum anti-Mullerian hormone (AMH) and antral follicle count (AFC) [11].

Ovarian reserve testing, by serum measurement of AMH, is not presently recommended as a population-based screening test for young women though it is being increasingly discussed in medical circles [12]. The potential ethical and clinical impacts of AMH testing are complex and multifaceted. Studies have shown that, if empowered with their individual ovarian reserve status, the decisions women make regarding further education and career may be different. It is argued that if a woman is unexpectedly informed of a low AMH result indicating low ovarian reserve, she may choose to prioritize getting pregnant sooner or proceed with oocyte vitrification rather than focus on career progression immediately [13,14].

Surprisingly, we are not aware of any studies addressing the psychological impact of having an AMH assessment. A poor result could have potentially devastating psychological and social sequelae. It is likely that these concerns are underestimated by health care staff because current standard practice does not include the provision of any pre-test counselling. Ovarian reserve assessments are often prompted due to subfertility which is known to cause severe psychological distress, affecting self-esteem and relationships with others [15]. This may further add to the psychological impact of a low AMH result.

In the absence of studies evaluating the psychological impact of ovarian reserve testing, we focused our literature review on premature ovarian failure. Women diagnosed with premature ovarian failure report higher levels of depression and perceived stress, and lower levels of self-esteem and life satisfaction, compared to the general population [16]. Self-reports on several dimensions of sexuality were significantly more negative [16]. One study concluded that women who receive a diagnosis of premature ovarian failure often feel that their lives are "out of synchrony" [17]. In a cross-sectional study, women who were diagnosed with primary ovarian insufficiency, compared to controls, scored adversely on all measures of affect, supporting the need for further prospective studies [18].

Groff et al examined the support structure that women used for coping following the diagnosis of premature ovarian failure [19]. They reported high levels of dissatisfaction relating to how patients were informed of the diagnosis and this impacted on the degree of emotional distress experienced by women. Participants in the study also found that access to accurate medical information, support of others and spirituality helped in coping [19].

In keeping with the views of most reproductive medicine specialists, the authors agree that significant medical benefits could derive from universal AMH screening for women in their mid to late twenties. Knowledge of a low ovarian reserve status may help women to choose to prioritize motherhood earlier than planned, or to consider oocyte vitrification, at a time where they have a reasonable chance of success, in an effort to avoid unintended childlessness due to delayed childbearing [13,14].

However, we also contend that it may be unethical to introduce such screening without first elucidating its likely psychological and emotional impact. The aim of this study was to investigate the emotional and psychological responses of women to receiving their AMH result and to identify measures that health professionals could adopt to ameliorate any negative impact.

Materials and methods

Study design

The study took place in Merrion Fertility Clinic which is a tertiary referral reproductive medicine centre in Dublin, Ireland. A purposive sample was chosen of women who had had a serum AMH level tested as part of their gynecological investigations. The primary investigator identified from the biochemistry laboratory database individuals who had AMH testing performed in the previous three months and had been reviewed by a clinician to inform them of the result. This was the only inclusion criteria as this was a pilot qualitative study. We purposively sampled participants of varying ages and AMH levels to enable a global and encompassing perspective of different individuals. This approach allowed for experience across several different factors to be explored. Eligible patients were contacted by telephone to invite them to participate in the study. This contact was facilitated by an opt-out option on a baseline patient demographics form which they had completed on first contacting the clinic. Patient information leaflets and consent forms regarding the study were then posted to interested individuals. Written consent was obtained prior to all interviews. Interviews were continued until thematic saturation had been achieved – this is defined as the ongoing collection and analysis of data until no new information is obtained.

Participants

Ten women were interviewed between February and April 2016. Participants' ages ranged from 24 to 36 years.

Five of the women had an AMH result less than the 10th centile indicating low ovarian reserve, three had a normal AMH result (10–90th centile) and two women had an AMH result greater than the 90th centile, most likely indicating polycystic ovarian morphology (As per Roche AMH assay reference ranges). Eight women were actively trying to conceive. One participant with endometriosis had the test performed pre-operatively and the remaining woman had availed of the test opportunistically. Three of the women had been pregnant previously but only one had had a live birth. One of the study participants was pregnant at the time of the interview. Data saturation was reached after 10 interviews.

Data collection

Data were collected through in-depth, semistructured interviews allowing the identification of key areas of interest while also facilitating the exploration of information and ideas that are important to the participant. The semistructured interview can be viewed in appendix 1. The interviews were audiotaped and ranged in duration from 15 to 30 min. Interviews were conducted at Merrion Fertility Clinic by the lead author (YOB). The interviewer (YOB) was trained in the use of the interview guide as a tool by one of the co-authors (CK). Interviews were transcribed verbatim by the lead author, anonymized with fictitious names and imported into the NVivo pro 11 software package for analysis.

Data analysis

Braun and Clarke's guide to thematic analysis was used to analyze and code the transcripts. They describe thematic analysis as "A method for identifying, analyzing and reporting patterns within data" [20]. Themes are recurring ideas across different data sets that are important and central to the description of an event addressing a specific research question. The primary investigator (YOB) performed open coding on all transcripts to derive a list of themes after reading transcripts several times to enable familiarity. Once complete, the initial codes were reviewed and discussed with one of the co-authors (CK) before being revised and finalized. Initially, 180 separate codes were generated which were then arranged into categories and subcategories, representing specific themes. Using axial coding, three key themes were identified and are detailed below accompanied by illustrative quotes.

Ethical approval

This study was approved by the Medical Research and Ethics committee of the National Maternity Hospital, Holles Street, Dublin, affiliated with Merrion Fertility Clinic (Reference EC 05.2016, 12th January 2016). Participants were aware they could decline to be interviewed, were guaranteed confidentiality and were not given any incentives to take part in the study.

Results

Ten women were interviewed between February and April 2016. Participants' ages ranged from 24 to 36 years. Five of the women had an AMH result less than the 10th centile indicating a low result, three had a normal AMH result (10th–90th centile) indicating satisfactory ovarian reserve and two women had an AMH result greater than the 90th centile, most likely indicating polycystic ovarian morphology. Eight women were actively trying to conceive, and this was the indication for ovarian reserve testing. One participant with endometriosis had the test performed pre-operatively and the remaining woman had availed of the test opportunistically. Three of the women had been pregnant previously but only 1 had had a live birth. One of the women was pregnant at the time of the interview, after she had had the AMH test. All the patients were interviewed within three months of the blood test and at least two weeks since the medical review when they got their result. Data saturation was reached after 10 interviews. This study revealed three major themes: the experience of AMH testing, the response to AMH results, and lessons for healthcare professionals.

Experience of AMH testing

The theme of the experience of AMH testing describes and reflects two sub-themes: the reasons for ovarian reserve testing; and the potential barriers that may prevent women from accessing testing.

Reasons for testing

For the majority of women in this study, the AMH test was performed as part of routine fertility investigations at the clinic. Women had been trying to conceive for between eight months and three years:

> *"I had been trying for about two and a half – three years and my doctor suggested maybe I get some bloods done" – Sophie aged 24, Low AMH*

In other participants, being indirectly affected by infertility through knowing someone who had experienced infertility issues themselves was, the stimulus for testing

"Myself and my husband had decided that we had been trying for about 8 months or so, and we weren't finding ourselves pregnant… … ….my husband's brother, he had problems, and they'd been unable to have children so far. So we decided we would come in and get an initial check"- Marie aged 33, Normal AMH

One woman reported that she had the test after hearing a radio advertisement offering "Free AMH" testing.

"Well I went to X clinic I think last year when they were doing a campaign on making people more aware of AMH, of fertility testing. They were doing a free AMH test and then I think they got overwhelmed so then they did a half price [offer], so I got it for half price."- Naomi aged 30, Low AMH

Barriers or obstacles to testing

For some women who may have delayed presenting for investigation, one of the most common reasons they gave was a fear of negative results. Some identified this as a self-preservation technique that by not proceeding with testing, they were protecting themselves from a potentially low result.

"I think I was a bit afraid to go and get tested in case it came back with negative results that we didn't want. So there was an element of fear stopping us to move in the right direction"- Sophie aged 24, Low AMH

Another possible barrier to accessing ovarian reserve testing was the lack of awareness that such a test existed. Many believed they would have sought ovarian reserve testing sooner if they had been aware of it.

"And obviously having that test as well, I would have started earlier, rather than putting it off, yes absolutely. If 10 years ago I knew, we would have had children first"- Laura aged 33, Low AMH

Women who felt dismissed by their General Practitioner suggested this as the reason for delay in testing. They reported that their concerns were not being addressed by the General Practitioner due to age or current reproductive behaviour.

"You don't need to have that done, you're too young … I only go to her if I really need to, which is not a lot. I find her very dismissive"- Laura aged33, Low AMH

In summary, the major theme relating to the experience of AMH testing incorporated the women's reason for testing and the potential barriers toward testing. The main reason women had availed of the AMH test was that it was part of the routine set of investigations that were prescribed by the clinic, however they were often unaware of the importance or significance of the test until afterwards. Fear of an abnormal result was one of the barriers that was described by some women which delayed them accessing testing. Furthermore, the lack of awareness of this test amongst women was seen as a barrier in accessing testing. Many said that they would have accessed AMH testing sooner if they had been aware of the test.

Responses to AMH results

A key focus of this study was the emotional and psychological responses to receiving their AMH results and, as such, emerged as a major theme in the interviews. Women described the impact that their individual result had had on a number of lifestyle and behavioral factors and how it impacted on their gender identity.

Emotional and psychological responses

Women who received a result in keeping with normal reserve ranges ($n = 3$) recalled initial feelings of relief, happiness and confidence.

"she said it was 15, it was more of a relief… … Yeah happy and relieved"-Fiona aged 26, Normal AMH

"I was happy to know that that was one less hurdle to face"- Katie, aged 33, High AMH

Similarly, women who received an abnormally high AMH result, also did not report any significantly negative emotional responses to the result either initially or subsequently.

Several women who were informed of low ovarian reserve ranges reported some negative emotional and psychological responses on being given their results. For example, as one woman described

"I walked out of there like an absolute zombie. Devastated…. I was just heartbroken… … I sobbed the entire way home not knowing what to do"- Laura aged 33, Low AMH result

Other women described feelings of devastation at hearing the result and a sense of being "cheated" by not having had this information sooner as well as concerns about the impact that this result might have on their future reproductive plans. Some illustrative quotes below are presented below.

"When I got out, I had a bit of a meltdown… …. Devastated. Thinking "will we have kids"? That was the main thing"- Sophie aged 24, Low AMH

"I know that sounds a bit dramatic but you kind of feel a bit cheated or something, that you never knew, something like that… …At the start I was very pissed off about it. Kind of felt a bit cheated"- Hilda aged 33, Low AMH

One woman very powerfully described her reaction as being similar to reacting to a death and compared it with the different stages of grief:

"It kinda felt like a death or something like that cause I kinda went through the grief process or something. That you're kinda going angry, denial, all that kind of stuff going on"- Hilda aged 33, Low AMH

Perhaps indicative of this bereavement model of responding to the news one woman described a sense of acceptance;

"We are thankful for what we have and if we don't have children we have beautiful nieces and nephews around us. You have to kind of look at it a bit pragmatically I suppose"- Sinead aged 36, Normal AMH

While others, despite receiving a result indicating low ovarian reserve, reported that they were still happy to have the information and even that they felt empowered, as illustrated below

"I'm happy that I know. Definitely happy that I know"- Naomi aged 30, Low AMH

"Dr X was lovely….and we walked out of there not feeling "oh god this isn't going to work", it was more, we'll get it sorted"– Rachel aged 34, Low AMH

Outlook and behavioral modifications

Study participants discussed ways in which the AMH result had impacted them, in terms of their behavioral and lifestyle responses.

Fertility awareness and outlook. Many women made reference to the impact of the AMH result on their awareness of fertility and reproductive behavior.

"Definitely more aware. I wouldn't now be putting off starting a family until I was 36 or 38 cause I know if I was tested for AMH at that time it could be down to 0"- Naomi aged 30, Low AMH

Women described themselves as becoming more realistic regarding their expectations of fertility treatment as a result of AMH testing. They felt that having this information relating to ovarian reserve better prepared them for the potential outcome of treatment, aware that it may not work.

"We're going into it [IVF treatment] with our eyes open; we know my level is low. We're going in with our eyes open. We're not like this is the answer and it'll work straight away. We both know it mightn't work"- Hilda aged 33, Low AMH

Loss of femininity and sense of stigma. The impact of AMH testing on a woman's self-image and her sense of femininity was evident.

"It made me feel kind of like less of a woman or something, like I couldn't reproduce properly"- Hilda aged 33, Low AMH

Furthermore, even when the result was normal for their age group, one woman still looked on her result as a "stigma". The stigma was in relation to the fact that she needed to have the investigation performed in the first instance.

"She said it was 15, it was more of a relief but I also felt that it was kind of a stigma."- Fiona aged 26, Normal AMH

In summary, the impact of AMH testing on a women's emotional and psychological wellbeing is significant. The women who received a normal result expressed feelings of happiness and relief. The women who received a result indicating a low ovarian reserve described feelings such as devastation and grief. Notably, even those women who described such strong negative emotional states were still happy they had the test performed as they now felt empowered with knowledge they could act upon. Regardless of the result, the impact of the idea of testing evoked powerful questioning on femininity and the stigma surrounding subfertility.

Lessons for healthcare professionals

Participant awareness, understanding and pretest expectations of ovarian reserve testing

Women were asked about their understanding of AMH. Many women correctly interpreted AMH testing as a marker of ovarian reserve and not necessarily reflective of fertility.

"That it [AMH] was just a measure of egg reserves but that it doesn't really tell you too much about whether you're going to have too much difficulty or not getting pregnant"- Emer aged 33, High AMH

They were often disappointed by the level of knowledge the General Practitioner had in relation to the AMH test.

"My GP had to google it. She didn't have a clue"- Naomi aged 30, Low AMH

Some women were very aware of the misconceptions regarding testing in the general population. They, at times, tried to educate their friends.

"I remember having a detailed discussion with a group of friends of mine, no one is medically trained, one of the girls was saying "we should all get our AMH levels tested", and I was like I don't really think it's going to tell you much. It's going to tell you certain things but I don't think it really tells you whether you're going to

have loads of problems or not" - Emer aged 33, High AMH

Prior to testing, many women had assumed a normal result. This was especially pronounced if they had a normal menstrual cycle or a family history of proven fertility.

"It never crossed my mind that there would be anything wrong … … … because I had such regular periods, I thought everything was tickety-boo … I didn't expect it at all"- Hilda aged 33, Low AMH

Conversely, many women had prepared themselves for an abnormal AMH result. They described it as a self-preservation technique.

"I had anticipated a low result in my head so that if it came back low I wouldn't be so shocked."-Fiona aged 26, Normal AMH

Communication of the result

Staff competence, attitude and means of communicating the result emerged as significant factors influencing the experience of AMH testing. Positive experiences related to the proficiency of the doctor in being able to explain the result in terms appropriate to the woman. The language the doctor used in communicating the result was very important.

"I was happy with it. It was kind of broken down in layman's terms to be honest with you"- Marie aged 33, Normal AMH

Women responded well to the additional aids the doctor used in order to communicate the result and its interpretation.

"She actually drew it out on a piece of paper explaining exactly what it meant"- Hilda aged 33, Low AMH

Some women described their experience of receiving the result in a negative light. Contributory factors included inappropriate timing and location of communication of the result. One woman was given her result on the day of her surgery.

"I got told the result by Dr X. It was just before or after the operation, I can't remember. I suppose it could have been explained a bit better and maybe to provide a patient information leaflet for somebody who's after an operation and sedation"- Fiona aged 26, Normal AMH

One woman was communicated the result whilst driving.

"I was actually driving at the time, typical. So I couldn't take in too much, she told me and I said ok fine, it was on Bluetooth, and she asked me one or two things but I couldn't really take it in, cause I was driving, so it was only afterwards that it hit home a bit"- Naomi aged 30, Low AMH

Universal AMH screening

To further explore the area of universal AMH screening, we asked the participants about the advantages and disadvantages of AMH testing. Many women felt that receiving knowledge of their AMH level, regardless of the result, was extremely positive and valued this new individualized information.

"Oh God, there is advantages of it because you know, you know then that there is something that you need to address, you need to be aware of it, that there's an issue there … You may not like the results but at least you know what's going on"- Hilda aged 33, Low AMH

Knowledge of AMH results was also very beneficial for women who felt it had contributed positively to their decision-making as regards childbearing intentions.

"I think all knowledge is power. If I didn't know, I wouldn't up my timeline. I would still hold off until 35. So at least now, knowing what they are, it gives me a chance to readjust everything … . instead of waiting for another year and a half, six months is my timeline now and if not by then, start earlier with IVF"- Laura aged 33, Low AMH

Some women were critical about ovarian reserve testing. Their criticisms included the unnecessary worry and stress that it created, the sense of urgency and haste toward fertility treatment that resulted and the effect of the result on a person's self-image in relation to sense of femininity and the social pressures of constant comparison.

"But sometimes you think - was I looking into all this and I could have been fine? Who knows? That's the other side of it … … everything could be fine if you didn't know."- Naomi aged 30, Low AMH

There was some support for the introduction of AMH testing as a screening tool for all women.

"I think the majority of women will still have all their eggs in a basket at 20 or 30, but I think everybody should have it, every woman should be offered it"- Laura aged 33, Low AMH

However the majority of the study participants felt that testing should be reserved for certain groups of women, depending on their social circumstances. Relationship status, current childbearing intentions and reproductive choices were factors raised.

"If you're not trying to conceive, I wouldn't imagine there would be much of point [of ovarian reserve testing]."- Rachel aged 34, Low AMH

In summary, there were many lessons for health care professionals to be learnt. Firstly, the need for the

physician to engage with the patient and assess their level of knowledge is key to the clinical interaction. Their manner, their communications skills, the use of aids and the location and setting of the clinical interaction has a profound impact on the how the patient deals with the result. In relation to their opinions on the introduction of universal AMH screening in the general population, the majority of women in our study feel that AMH testing should be reserved for certain groups of women who have a clinical need for AMH testing as it has the potential to create unnecessary distress and urgency for women who are not in a position to conceive presently.

Discussion

This study has explored for the first time, to our knowledge, the psychological and emotional impact of AMH testing. When offering any investigation or treatment, healthcare professionals need to be cognisant of the implications of their actions or advice. Clinicians must evaluate, on the one hand their commitment to benefit the patient (the principle of beneficence) but also their commitment to cause no harm (the principle of non-maleficence) [21].

Our findings suggest that AMH testing can have a significant emotional and psychological impact on an individual. Emotions were generally reflective of the result, but not always. Testing provoked a sense of stigmatism and lack of femininity for some individuals, regardless of the result. These feelings were linked with fears of not being able to conceive. Some women were heartbroken and devastated by a low result and what it might mean for their ultimate life plans. The fact that one woman described it as a grieving process was very powerful. Indirectly, she may be grieving for the biological children she may now not be able to have. This sense of loss or grief has been described previously in women diagnosed with premature ovarian failure [22]. As healthcare professionals, we must acknowledge the significant stigma and loss of femininity that fertility testing, and possible unintended childlessness can evoke for an individual.

Significant benefits have also been mentioned by our study participants. Women greatly valued the information they received, regardless of the result. As one woman stated: "Knowledge is power". A personalized risk assessment has the potential to have a much stronger impact on individual action and behavior modification than just generic advice [12]. When given a low AMH result, the study participants adjusted reproductive goals and timelines. Some even mentioned that if others were similarly informed, they could consider fertility preservation options such as egg freezing. The demand for egg freezing or oocyte vitrification for delayed childbearing, from an Irish perspective, is driven by the patient currently as there is no public funding for this treatment presently.

This study identified key areas and lessons for healthcare professionals in relation to the education of patients and communication of results. As in previous studies, the manner in which the result and its interpretation are communicated to the patient have the potential to significantly impact her level of distress [19]. Furthermore, women who were unfamiliar with the test felt they were "bombarded with too much information". This is an important learning point. Prior to informing the patient of the result, some attempt must be made to assess the woman's knowledge. This is likely to improve the discussion and lead to a more productive clinical consultation. Ideally, communication of the result (irrespective of the value) should take place during a face to face consultation with sufficient time to enable interpretation of the result. For some women, who receive bad news, extra consideration should be given to extending the length of the consultation to fully address their needs.

The findings from this study are limited by its retrospective nature. Recall bias may be a significant component. Some of the women, particularly if informed of a low result, may not have accurately remembered the details of the consultation as they were so upset at the time. We therefore cannot generalize the results of the study. However, important information with regard to the impact of AMH testing on an individual has been assessed for the first time.

In conclusion, this study has furthered our evidence base with regard to the ethical considerations surrounding the introduction of ovarian reserve testing for the general population. By evaluating the social context of a low AMH result, this study helps to identify factors that can facilitate or hinder an individual's health seeking behavior and acceptance of the result. These factors include pre-existing knowledge and awareness of the patient in relation to AMH testing, fear or abnormal results and furthermore the awareness of their General Practitioner of AMH testing and its significance. Additional knowledge of AMH level will certainly aid strategies to prevent unintended childlessness as a result of premature reduced ovarian reserve. However, care must be taken to "do no harm" in the process. We must respect patient autonomy and educate, inform and empower women with regard to their request to seek a personalized risk assessment which could potentially modify their behavior.

The results of this initial qualitative study will be used to develop a detailed quantitative questionnaire for the next stage of this investigation. However, it is already clear that the psychological and emotional impact of AMH testing must be carefully considered by all of those working in the field.

Disclosure statement

The authors report no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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➢ Current knowledge on this subject

- There is no studies specifically addressing the impact of AMH testing. A semistructured interview schedule was developed after a review of the literature regarding the diagnosis of premature ovarian failure.