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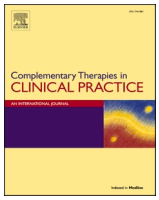

# Establishing key components of naturopathic management of women with diminished ovarian reserve: A Delphi study

Alison Maunder [a,*], Susan Arentz [a], Mike Armour [a], Michael F. Costello [b], Carolyn Ee [a]

[a] NICM Health Research Institute, Western Sydney University, Penrith, NSW, Australia
[b] Women's Health, UNSW and Royal Hospital for Women and Monash IVF, Sydney, NSW, Australia

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## 1. Introduction

Diminished ovarian reserve (DOR) is a gynaecological disorder characterized by poor fertility outcomes as a result of fewer oocytes in the ovaries compared to other women of the same age. While a decrease in ovarian reserve is a normal part of ageing, some women experience a decrease beyond what is physiologically expected due to normal age-related decline [1].

It is widely estimated that DOR affects ten percent of women seeking medically assisted reproduction (MAR) treatment. MAR is the first-line treatment for women with DOR, however the success rate is significantly lower than in women with normal ovarian reserve [2]. Women with DOR undergoing ovarian stimulation have an increased risk of ovarian hypo-response, high rates of cycle cancellation, high use of ovulation stimulants, low number of collected oocytes, low embryo numbers and low clinical pregnancy rates compared to women with normal ovarian reserve [3–5]. Further, the high cost and inequity of access to MAR treatment have been well reported [6].

Given the time constraints on a woman's ability to conceive, and the limited options available, complementary options are frequently sought. Many women in Australia use traditional, complementary and integrative medicine (TCIM) to improve their chances of having a live healthy baby [7,8] with women attempting to conceive more likely to consult with a naturopath than women who are not trying to conceive [9]. Reasons for seeing a naturopath include a desire to conceive spontaneously, to maximise the chance of success of MAR treatment or to explore options after MAR has failed [7,10,11]. However, despite high rates of use, there is no evidence that naturopathy for fertility as it is provided in the community will improve reproductive outcomes. Potential risks include lost opportunity for successful MAR given the time delays associated with naturopathic care. Whilst there is no evidence that women use naturopathy as an alternative replacement for standard medical care, the aim to optimise pre-conception health before conception (a principle of naturopathic practice), may delay women seeking conventional medical care. In addition, other risks include interactions of the naturopathic treatments with MAR pharmaceuticals and the safety of the naturopathic treatments.

Naturopathy is a system of healthcare that has evolved from a combination of traditional practices and health care approaches originating in Europe in the 17th century [12]. Whole-system naturopathy refers to the practice of naturopathy as a complex intervention based on holistic clinical decision-making which utilises a combination of clinical modalities adapted to suit individual needs [13]. A typical naturopathic consultation may involve counselling, shared decision-making, clinical examinations, with strategies to achieve clinical outcomes including self-care practices, mind-body therapies, manipulative therapies, ingestible and topical medicines [13,14]. The variety of strategies and techniques in a typical consultation demonstrates how naturopathy is a complex intervention as it comprises a number of different components and practices that each may contribute towards the therapeutic outcome with a high degree of flexibility in its clinical application [15].

To be able to investigate the effectiveness of whole-system

* Corresponding author. NICM Health Research Institute Western Sydney University Penrith Campus, Locked Bag 1797, Penrith, NSW, 2751, Australia.
*E-mail address:* alison.maunder@westernsydney.edu.au (A. Maunder).

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naturopathy for women with DOR, it is important to understand the key components of naturopathic management prior to these being tested in a clinical trial. The Delphi technique enables consensus building via an iterative survey process, while providing anonymity, equality of participant views and overcomes geographical differences. It provides a rigorous process to gain consensus on a complex intervention by using experts who are likely to use the interventions in question [16]. The aim of this Delphi study is to describe naturopathic management of women with DOR and guide development of a naturopathic intervention to be investigated in future randomised controlled trials (RCTs).

## 2. Materials and methods

### 2.1. Design

This study was designed and conducted using a Delphi technique, with reference to previous Delphi studies in the TCIM field [17]. The Delphi technique is a method of gaining consensus on a particular topic through the use of multiple rounds of questioning of experts in the field and was used because it allows anonymous group interactions and responses, and the provision of feedback to the group between each round of questioning [18]. The on-line platform and asynchronous timing suits busy practitioners, different time schedules and varied geographic locations [19]. The Delphi method provides a rigorous process to describe complex interventions by using experts who are likely to use the interventions in question [16].

The design, conduct and analysis of the Delphi survey was overseen by the authors (AM, SA, MA, CE) who were chosen for their combined representation of women's health research, naturopathy, TCIM research and Delphi methodology. The aim of the Delphi study was to guide the development of a naturopathic intervention to be investigated in a subsequent RCT. The Delphi study was piloted by three qualified Australian naturopathic practitioners to assess relevance, clarity of questions and time involved. The study was given ethics approval by the Western Sydney University Human Research Ethics Committee (H14256 March 2021).

### 2.2. Participant selection and recruitment

To ensure the Delphi outcomes would be relevant to naturopathic practice in Australasia, naturopaths from Australia and New Zealand currently practicing in the field of naturopathy and fertility were invited to participate in the Delphi study. An eligible expert was defined as having a qualification in naturopathy and at least two of the following

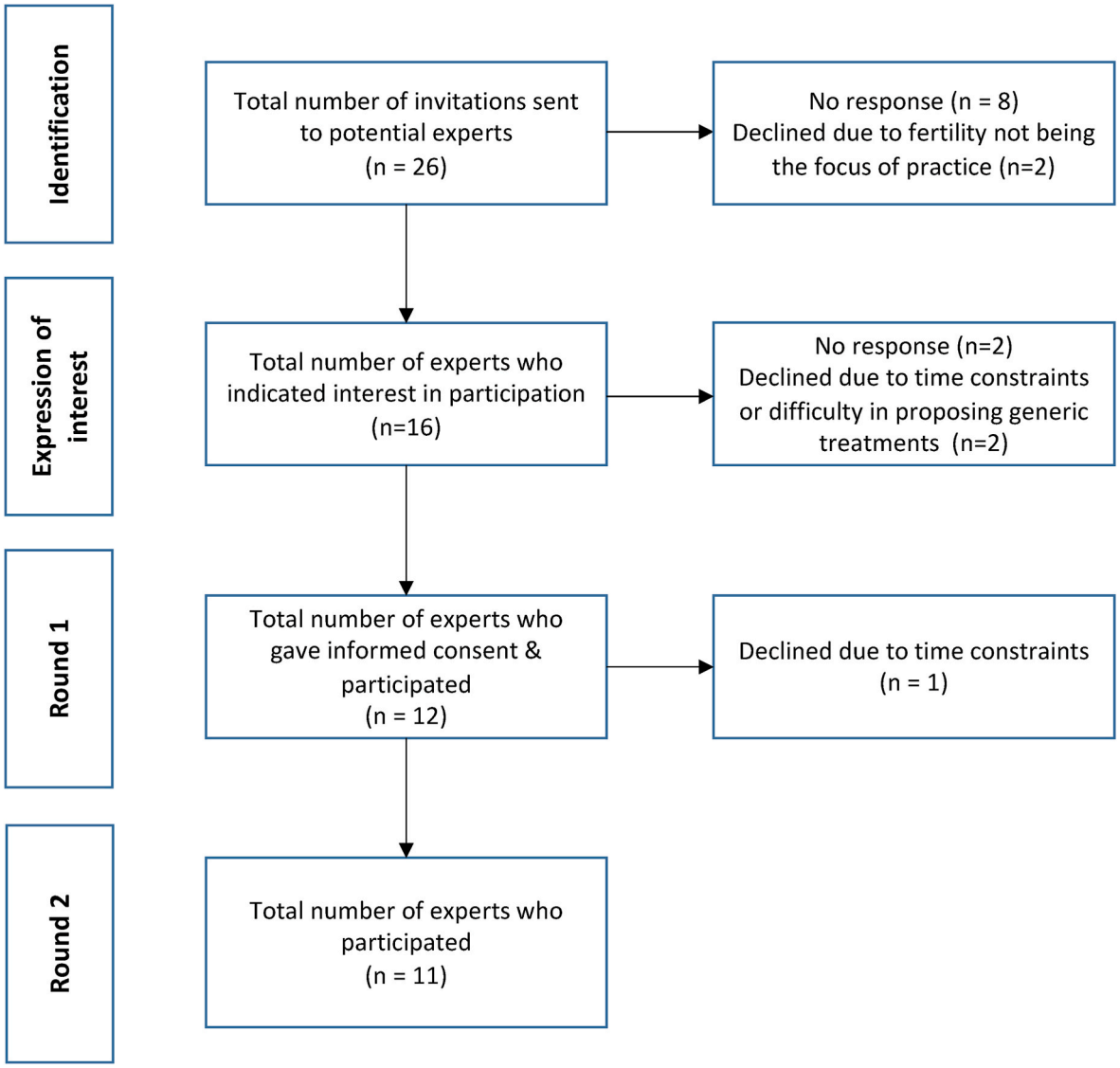


**Fig. 1.** Flowchart of participation in the two-round Delphi study.

criteria: (i) ten years' experience in treating women's reproductive health, (ii) post-graduate training in women's reproductive health, (iii) involvement in education of students or health professionals on naturopathic management for women's health conditions, and (iv) contributions to textbooks relating to naturopathic management of women's reproductive conditions. Members of the research team, who are familiar with the Australian naturopathic community, prepared an initial list of potential experts. This list was then augmented by potential experts recommending additional experts. All recruitment was conducted via email invitation using a standardised script for inviting experts. Formal consent was implied on completion of the first survey.

### 2.3. Sample size

There is no guidance on calculating sample sizes for Delphi studies, however, a generally accepted minimum suitable panel size is seven respondents [18]. Including more participants increases the variety of expertise but also increases the time to collect and difficulties in summarising the responses [16]. The sample size of 12 was determined by taking into account the estimated number of available experts and an expected 20–30 % drop-out rate in between rounds.

### 2.4. Procedure

We collected data in two rounds over a four month period from June to October 2021. On-line questionnaires were emailed to experts through a secure electronic link and responses were captured using Qualtrics$^{XM}$ v10.21 (Qualtrics, Provo, UT, USA). Experts were informed that formal consent was implied upon completion of the survey in the participant information sheet that was provided to participants before commencing the survey by an electronic link.

The first round Delphi questionnaire consisted of items grouped in five sections (additional file 1). The first section asked about appointments (e.g. duration, frequency and topics covered in consultations, the populations most indicated for naturopathic treatment, the use of a preconception period); the next three sections proposed different clinical scenarios and asked about naturopathic treatment of women with DOR in the following situations: (i) currently trying to conceive naturally, (ii) currently trying to conceive alongside MAR, (iii) not currently trying to conceive but wanting to in the future. Each of these three sections asked about key naturopathic treatments, including selection of the most utilised nutritional supplements and herbal medicines, dietary recommendations, timing and indicators of treatment review, clinical outcomes to be reviewed, expected time frames and a final free-text question for additional treatment considerations. The final section asked about demographics (gender, naturopathic qualifications, qualifications in reproductive medicine, years in practice, frequency of managing women with DOR) and included a free-text question for experts to comment or make suggestions about the study.

As per the iterative Delphi process, the first round of the survey was analysed when completed, with the results forming the content of the second round. Each survey took around 20–30 min to complete and consisted of 43 and 37 questions respectively. Experts were given two weeks to complete each round, with non-responders being sent two reminder emails. If no response was obtained in round 1, these experts were excluded from the subsequent round.

Individual items from the round one survey that reached consensus were summarised and presented as a proposal for the intervention in the round 2 survey inviting further comments or suggestions. Items that did not reach consensus and new items suggested by the experts were reworded for rating by using a Likert scale of agreement along with inviting comments or suggestions. Nutritional supplements and herbal medicines that were frequently selected by most experts in round one were summarised. Supplements and herbal medicines that were reported as being used occasionally or rarely by the experts were presented for rating by using a Likert scale of frequency of usage, in addition to free-text comments on dosage form and quantity.

**Table 1**
Expert demographics (n = 12).

| Characteristic | | n (%) |
|---|---|---|
| Gender | Female | 12 (100) |
| Country of practice | Australia | 10 (83) |
| | New Zealand | 2 (17) |
| Highest qualification in naturopathy | Bachelor degree | 9 (75) |
| | Diploma/Advanced diploma | 3 (25) |
| Additional qualifications related to women's health | Master degree | 2 (17) |
| | Graduate Diploma in Natural Fertility Management | 7 (58) |
| | Midwifery | 1 (8) |
| Years in practice | 10–19 | 7 (58) |
| | 20–29 | 2 (17) |
| | More than 30 | 3 (25) |
| Frequency of patients with DOR | More than 10 per week | 2 (17) |
| | 4–6 per week | 1 (8) |
| | 1–3 per week | 3 (25) |
| | Not every week, but every month | 3 (25) |
| | Not every month | 3 (25) |
| Type of practice | Multi-disciplinary practice with other health practitioners | 6 (50) |
| | Multi-disciplinary practice with medical practitioners | 2 (17) |
| | Practice with other naturopaths | 2 (17) |
| | Solo practitioner | 2 (17) |

DOR = diminished ovarian reserve.

### 2.5. Analysis and consensus

Consensus was assessed as collated frequency per response category and percentage of each rating of agreement. Level of consensus was measured as the number of ratings given in each response category. We defined *general consensus* as 75 % or more of experts rating in a particular response category. Results are reported as a summary of consensus from both rounds of questionnaires.

## 3. Results

### 3.1. Recruitment

Twenty-six potential experts were identified through the recruitment process between June and October 2021 and invited to participate; of these 16 (62 %) expressed an interest to participate in the Delphi study (Fig. 1). From these 16 experts, 12 (75 %) consented to participate in the Delphi study and completed the first survey (10-Australia, 2-New Zealand), two did not respond, one declined to participate due to time constraints and one declined to complete the survey due to the difficulty in proposing generic treatments. Eleven experts (92 %) (9-Australia, 2-New Zealand) completed the second round and one declined to participate due to time constraints. Table 1 describes the demographics of the experts.

#### 3.1.1. Delphi rounds

In the first section of the Delphi study, consensus was reached in the categories regarding appointment duration, frequency, topics covered in consultation, most relevant population, and the use of a preconception period (Table 2). For the topics to be covered in an initial consultation, 14 topics were agreed upon in the first round and a further six topics in the second round of the Delphi. For the topics to be covered in a follow-up consultation, four topics reached consensus in round 1 and a further four in round 2. The time between appointments varied but a consensus was reached in the second round to be four to six weeks apart.

In the next three sections (different scenarios of women with DOR according to their desires to conceive), consensus was reached for each

**Table 2**
Final consensus on naturopathic practice approaches for treatment of women with DOR.

| Consultation | | Round | n (%) |
|---|---|---|---|
| Initial consultation | 60–90 min | 1 | 10 (83) |
| Follow-up consultation | 45 min | 1 | 9 (75) |
| | 4–6 weeks apart | 2 | 9 (82) |
| Those to gain most benefit from naturopathic treatment | Conceiving naturally – all ages | 1 | 10 (83) |
| | Concurrent treatment with MAR – all ages | 1 | 11 (92) |
| Reason to recommend against avoiding conception for a "*preconception period*"* | "Time left for conception is too short" | 1 | 11 (92) |
| | "Patient's preference" | 1 | 9 (75) |
| Topics to be discussed in an initial consultation | **History** | | |
| | Reproductive health history (fertility history, co-morbidities/complications, medical management and interventions, partner's health) | 1 | 12 (100) |
| | Menstrual cycle history, symptoms, ovulation | 1 | 12 (100) |
| | Medical history | 1 | 12 (100) |
| | Family history | 1 | 12 (100) |
| | **Current health** | | |
| | Psychological and emotional status (stress, fears) including partner in support strategies | 1 | 11 (92) |
| | General health | 1 | 11 (92) |
| | Current medicines including pharmaceuticals, nutritional supplements and herbal medicines | 1 | 9 (75) |
| | **Diet & Lifestyle characteristics** | | |
| | Diet | 1 | 11 (92) |
| | Lifestyle including exercise, leisure activities, alcohol/drug use | 1 | 11 (92) |
| | Sleep patterns | 1 | 11 (92) |
| | Digestion, assimilation & elimination function | 2 | 11 (100) |
| | Physical characteristics including fingernails, tongue, blood pressure, weight, height, waist circumference | 2 | 11 (100) |
| | **Reproductive risk assessment** | | |
| | Including age, lifestyle factors, toxic exposures including chemical and radiation | 1 | 9 (75) |
| Topics to be discussed in a follow-up consultation | Assess current health including psychological and emotional status | 1 | 11 (92) |
| | Review timing for conception attempts or outcomes of treatment | 2 | 11 (100) |
| | Review last treatment plan to identify and discuss barriers and facilitators to support positive change | 1 | 11 (92) |
| | Cover any areas of initial consultation not covered | 1 | 11 (92) |
| | Review and discussion of any questionnaires completed (such as diet and symptom diaries) | 1 | 10 (83) |
| | Review and discussion of pathology results. Referral for previously unidentified pathology testing, if indicated. | 1 | 10 (83) |
| | Review and discussion of menstrual cycle charting. | 2 | 11 (100) |
| | Write referral letters to medical providers or respond to letters, as required. | 2 | 11 (100) |

DOR = diminished ovarian reserve, MAR = medically assisted reproduction, * a period of time to avoid conception.

**Table 3**
General consensus on key treatment aims for women with DOR.

| Key treatment aims | CS | Round 1 (n = 12) n (%) | Round 2 (n = 11) Order of priority 1 = highest |
|---|---|---|---|
| Optimise egg quality (increase antioxidants and upregulate mitochondrial function) | 1 | 8 (66.6) | 1 |
| | 2 | 10 (91.7) | 1 |
| | 3 | 8 (66.6) | 6 |
| Regulate menstrual cycle & ovulation (balance hormones; support follicular & luteal phases) | 1 | 9 (75.0) | 2 |
| | 2 | 2 (16.7) | – |
| | 3 | 9 (75.0) | 3 |
| Stress management (support nervous system and adrenal glands) | 1 | 7 (58.3) | 7 |
| | 2 | 9 (75.0) | 3 |
| | 3 | 8 (66.6) | 5 |
| Optimise nutrient dense diet, high in antioxidants | 1 | 7 (58.3) | 3 |
| | 2 | 5 (41.7) | 4 |
| | 3 | 5 (41.7) | 2 |
| Correct nutritional deficiencies (including methylation support) | 1 | 5 (41.7) | 4 |
| | 2 | 3 (25.0) | 2 |
| | 3 | 4 (33.3) | 4 |
| Include male partner in strategies to maximise general health and quality & volume of sperm | 1 | 6 (50.0) | 5 |
| | 2 | 1 (8.3) | 8 |
| | 3 | 0 (0.0) | – |
| Support ovarian tone & circulation | 1 | 3 (25.0) | 8 |
| | 2 | 3 (25.0) | 5 |
| | 3 | 3 (25.0) | – |
| Improve general health and well-being | 1 | 1 (8.3) | 10 |
| | 2 | 1 (8.3) | 8 |
| | 3 | 5 (41.7) | 1 |
| Support uterine health/tone/circulation & endometrial receptivity | 1 | 5 (41.7) | 6 |
| | 2 | 8 (66.6) | 7 |
| | 3 | 1 (8.3) | – |
| Inform about lifestyle and environmental factors that may promote fertility | 1 | 8 (66.6) | 9 |
| | 2 | 5 (41.7) | 6 |
| | 3 | 4 (33.3) | 7 |
| Inform about DOR and trying for pregnancy sooner or fertility preservation | 1 | 0 (0.0) | – |
| | 2 | 0 (0.0) | – |
| | 3 | 2 (16.7) | 8 |

Clinical scenarios (CS): #1 Trying to conceive (TTC) naturally, #2 TTC with medically assisted reproduction (MAR), #3 Not currently TTC; DOR = diminished ovarian reserve.

scenario for therapeutic objectives (Table 3) and measurements to assess clinical outcomes from treatment (Table 4). Similarly, the dietary recommendations reached consensus regardless of the clinical scenarios. All experts agreed that a Mediterranean diet would be the most frequently recommended diet for this population; this was closely followed by the recommendations to eat wholefoods and include organic foods (Table 5). Consensus was reached on nutritional supplements and herbal medicines. Of the 15 nutritional supplements that were proposed in round one, B complex vitamins and co-enzyme Q10 (and its derivatives) were found to be frequently recommended supplements. Following round two, six supplements had reached consensus for all scenarios (Table 6). The two herbal medicines that reached consensus in round one for the most often prescribed were *Vitex agnus-castus* (Chaste tree) and *Withania somnifera* (Withania) for women with DOR trying to conceive. During round two a further seven herbal medicines were agreed upon as often or sometimes prescribed (Table 7), however,

**Table 4**
General consensus on measurements to assess clinical outcomes from treatment for women with DOR.

| Recommendations | CS # | Round 1 (n = 12) n (%) |
|---|---|---|
| Measurement of basal follicle stimulating hormone (FSH) and/or oestrogen for comparison | 1 | 12 (100.0) |
| | 2 | 8 (66.6) |
| | 3 | 7 (58.3) |
| Measurement of mid-luteal progesterone for comparison | 1 | 11 (91.7) |
| | 2 | 11 (91.7) |
| | 3 | 4 (33.3) |
| Menstrual cycle regularity | 1 | 12 (100.0) |
| | 2 | 8 (66.6) |
| | 3 | 12 (100.0) |
| Menstrual cycle chart shows ovulation | 1 | 8 (66.6) |
| | 2 | 6 (50.0) |
| | 3 | 6 (50.0) |
| Improved results from MAR treatment | 2 | 12 (100.0) |
| Positive pregnancy test | 1 | 10 (83.3) |
| | 2 | 12 (100.0) |
| On-going pregnancy from 12 weeks | 1 | 12 (100.0) |
| | 2 | 12 (100.0) |
| On-going pregnancy from 20 weeks | 1 | 7 (58.3) |
| | 2 | 11 (91.7) |
| Live birth | 1 | 10 (83.3) |
| | 2 | 11 (91.7) |
| General well-being | 1 | 8 (66.6) |
| | 2 | 9 (75.0) |
| | 3 | 12 (100.0) |
| Health improvements | 1 | 9 (75.0) |
| | 2 | 9 (75.0) |
| | 3 | 12 (100.0) |
| Psychological improvement | 1 | 8 (66.6) |
| | 2 | 9 (75.0) |
| | 3 | 11 (91.7) |
| Improved body composition | 1 | 4 (33.3) |
| | 2 | 7 (58.3) |
| | 3 | 9 (66.6) |
| Measurement of anti-Mullerian hormone (AMH) for comparison | 1 | 4 (33.3) |
| | 2 | 1 (8.3) |
| | 3 | 2 (16.7) |
| To be reviewed at the follow-up appointment or between 1 and 3 months | 1 | 11 (100.0) |
| | 2 | 11 (100.0) |
| | 3 | 9 (81.8) |

Clinical scenarios (CS): #1 Trying to conceive (TTC) naturally, #2 TTC with medically assisted reproduction (MAR), #3 Not currently TTC; DOR = diminished ovarian reserve.

secondary herbal medicines used as part of a formulation were not agreed upon (Table 8).

## 4. Discussion

This two-round Delphi study is the first study to describe how naturopaths treat women with DOR. It reflects the views of 12 naturopathic experts and informs recommendations for the naturopathic management of women with DOR. In this study, consensus was reached for consultation characteristics, topics discussed at consultations, treatment aims, clinical outcomes, dietary patterns, and supplementation of nutrients and herbal medicines.

Consultation timeframes that were agreed upon were 60 min (min) for initial consultations and 45 min for follow-up consultations. This consultation structure confers with those reported by the recent World Naturopathic Federation survey assessing the naturopathic profession worldwide where more than 80 % of respondents reported that initial naturopathic visits were 60 min in length and 50 % of respondents noted that follow-ups ranged from 30 to 45 min [20]. The extra time in a naturopathic consultation is used to take a full case history, explore the complex multifactorial needs of patients and provide an individualised approach to treatment [21]. Longer consultations have the potential to strengthen the patient-provider relationship by allowing a safe space for patients to speak freely, sharing of knowledge and involving patients' preferences in decision making [22,23].

**Table 5**
General consensus on dietary patterns recommended for women with DOR.

| | CS # | Round 1 (n = 12) n (%) |
|---|---|---|
| Mediterranean diet | 1 | 12 (100.0) |
| | 2 | 12 (100.0) |
| | 3 | 12 (100.0) |
| Wholefood diet | 1 | 11 (91.7) |
| | 2 | 11 (91.7) |
| | 3 | 11 (91.7 |
| Organic foods | 1 | 9 (75.0) |
| | 2 | 11 (91.7) |
| | 3 | 11 (91.7) |
| Gluten-free diet* | 1 | 8 (66.6) |
| | 2 | 8 (66.6) |
| | 3 | 6 (50.0) |
| Low glycaemic carbohydrates | 1 | 6 (50.0) |
| | 2 | 6 (50.0) |
| | 3 | 7 (58.3) |
| Dairy-free diet* | 1 | 7 (58.3) |
| | 2 | 6 (50.0) |
| | 3 | 6 (50.0) |
| Lower intake of animal protein and higher intake of vegetable protein | 1 | 4 (33.3) |
| | 2 | 5 (41.7) |
| | 3 | 6 (50.0) |
| High protein diet | 1 | 2 (16.7) |
| | 2 | 3 (25.0) |
| | 3 | 2 (16.7) |
| Low carbohydrate diet | 1 | 2 (16.7) |
| | 2 | 1 (8.3) |
| | 3 | 1 (8.3) |
| Vegetarian diet or vegan diet | 1 | 1 (8.3) |
| | 2 | 2 (16.7) |
| | 3 | 1 (8.3) |
| Ketogenic diet* or high fat diet | 1 | 2 (16.7) |
| | 2 | 1 (8.3) |
| | 3 | 2 (16.7) |

Clinical scenarios (CS): #1 Trying to conceive (TTC) naturally, #2 TTC with medically assisted reproduction (MAR), #3 Not currently TTC; DOR = diminished ovarian reserve, * when clinically relevant.

Our study findings indicate that naturopathic practitioners discuss a wide range of health topics with their patients. Naturopaths, like many TCIM practitioners, adhere to practices founded upon the philosophy of holism, which aim to treat the whole person [24,25]. This is evident by the topics to be covered in the consultations and treatment aims that do not focus solely on fertility. This research aligns with the prior findings of Steel et al. [26] that naturopathic practitioners worldwide discuss varied topics that commonly include stress management, sleep, physical activity, diet and nutrition.

The focus on education and empowerment of patients to take responsibility for their health as part of naturopathic treatment is evident from our study. These findings align with the research of Brosnan et al. [25] that TCIM user empowerment occurs through a salutogenic approach. This approach views wellness and illness on a continuum and identifies and promotes factors that move patients towards the wellness end of the scale [27]. Consultations that listen to and value patients' stories, incorporate surveillance with disciplining and productive effects oriented towards health promotion were seen as key factors to enable patient empowerment [25]. Further, naturopaths' approach to educating patients reflects shared decision-making practices by discussing rather than giving information [26].

Interestingly, a preconception care period was not recommended by the experts as part of the naturopathic intervention for women with DOR. Preconception health of prospective parents is increasingly recognised as an essential element to achieve healthy outcomes for their children [28]. For naturopaths, a preconception care period may range from one menstrual cycle to several. During this time, women avoid conception whilst working towards optimal health [29]. Most experts would utilise a preconception care period for three to four months to

**Table 6**
General consensus on nutritional supplements recommended for women with DOR.

| Nutritional supplements most often prescribed (round 1 n = 12) | CS # | n (%) | Prescribing frequency (round 2 n = 11) | n (%) | Type and/or Daily dosage (round 2 n = 11) | n (%) |
|---|---|---|---|---|---|---|
| Coenzyme Q10 (CoQ10) | 1 | 11 (91.7) | Often/Always | 11 (100.0) | Ubiquinol | 10 (83.3) |
| | 2 | 10 (83.3) | Sometimes | 0 (0.0) | Any form of CoQ10 | 1 (9.1) |
| | 3 | 9 (75.0) | Never/Rarely | 0 (0.0) | 300 mg | 3 (27.3) |
| | | | | | 600 mg | 7 (63.6) |
| | | | | | ND | 1 (9.1) |
| B complex vitamins | 1 | 10 (83.3) | Often/Always | 11 (100.0) | Activated B complex | 11 (100.0) |
| | 2 | 10 (83.3) | Sometimes | 0 (0.0) | Prenatal with activated Bs * | 11 (100.0) |
| | 3 | 10 (83.3) | Never/Rarely | 0 (0.0) | | |
| Fish oils | 1 | 6 (50.0) | Often/Always | 11 (100.0) | 2 – 3g ** | 7 (63.6) |
| | 2 | 3 (25.0) | Sometimes | 0 (0.0) | ND | 4 (33.3) |
| | 3 | 3 (33.3) | Never/Rarely | 0 (0.0) | | |
| Zinc | 1 | 4 (33.3) | Often/Always | 10 (83.3) | 25–50 mg | 6 (54.5) |
| | 2 | 4 (33.3) | Sometimes | 1 (9.1) | ND | 5 (45.5) |
| | 3 | 3 (25.0) | Never/Rarely | 0 (0.0) | | |
| Vitamin D | 1 | 4 (33.3) | Often/Always | 9 (81.8) | 1000–4000IU *** | 6 (54.5) |
| | 2 | 2 (16.7) | Sometimes | 2 (18.2) | ND | 5 (45.5) |
| | 3 | 3 (25.0) | Never/Rarely | 0 (0.0) | | |
| Vitamin C | 1 | 4 (33.3) | Often/Always | 9 (81.8) | 1–3 g | 6 (54.5) |
| | 2 | 3 (25.0) | Sometimes | 0 (0.0) | ND | 5 (45.5) |
| | 3 | 2 16.7) | Never/Rarely | 2 (18.2) | | |
| Vitamin E | 1 | 4 (33.3) | Often/Always | 8 (72.7) | 120–240 mg | 4 (33.3) |
| | 2 | 1 (8.3) | Sometimes | 3 (27.3) | ND | 7 (63.6) |
| | 3 | 3 (25.0) | Never/Rarely | 0 (0.0) | | |
| N-acetyl cysteine (NAC) | 1 | 5 (41.7) | Often/Always | 8 (72.7) | 1000–2000 mg | 5 (45.5) |
| | 2 | 5 (41.7) | Sometimes | 1 (9.1) | ND | 6 (54.5) |
| | 3 | 3 (25.0) | Never/Rarely | 2 (18.2) | | |
| Alpha lipoic acid (ALA) | 1 | 3 (25.0) | Often/Always | 6 (54.5) | 400–1200 mg | 4 (33.3) |
| | 2 | 2 (16.7) | Sometimes | 3 (27.3) | ND | 7 (63.6) |
| | 3 | 2 (16.7) | Never/Rarely | 2 (18.2) | | |
| Inositol | 1 | 3 (25.0) | Often/Always | 6 (54.5) | 4–6 g | 5 (45.5) |
| | 2 | 1 (8.3) | Sometimes | 4 (36.4) | ND | 6 (54.5) |
| | 3 | 2 (16.7) | Never/Rarely | 1 (9.1) | | |
| Nicotinamide (NMN, NAD+) | 1 | 3 (25.0) | Often/Always | 5 (45.5) | 50–800 mg | 4 (33.3) |
| | 2 | 2 (16.7) | Sometimes | 3 (27.3) | ND | 7 (63.6) |
| | 3 | 1 (8.3) | Never/Rarely | 3 (27.3) | | |
| Magnesium | 1 | 1 (8.3) | Often/Always | 8 (72.7) | 300–600 mg | 5 (45.5) |
| | 2 | 0 (0.0) | Sometimes | 2 (18.2) | ND | 6 (54.5) |
| | 3 | 5 (41.7) | Never/Rarely | 1 (9.1) | | |

Clinical scenarios (CS): #1 Trying to conceive (TTC) naturally, #2 TTC with medically assisted reproduction (MAR), #3 Not currently TTC; DOR = diminished ovarian reserve, ND = no data provided, * when TTC, ** depends on dietary intake, *** depends on deficiency.

build up general and reproductive health, correct nutrient deficiencies, improve the quality of eggs and support psychological resilience for most women trying to conceive, however, it would not necessarily be recommended for women with DOR. The reasons cited for this decision were that time left for conception was an important consideration and the ultimate choice should be made by the patient.

Naturopaths, in general, aim to improve birth rates, however other outcomes related to whole-person health are also incorporated. There is insufficient evidence for preconception health promotion and improvements in live birth rates, and/or reduced adverse events including miscarriage [30]. Accordingly, our findings indicate that the experts use a variety of clinical outcome measurements to assess their treatment of women with DOR. In addition to the measurements of live birth and pregnancy rates, proposed clinical outcomes included health improvements, general health and well-being, psychological well-being and menstrual cycle regularity. These findings align with other research that demonstrates TCIM practitioners are sought for their focus on well-being and preventative care which is often embedded in their modality [31]. Future research should aim to assess whether other health outcomes contribute to improved rates of fertility.

Dietary interventions were considered an important component for improving general health in women with DOR, and the most highly recommended diets were Mediterranean, wholefood and organic food diets. Diets high in mono and poly unsaturated fats, whole grains, vegetables, and fish, that are typical components of a Mediterranean diet, have been associated with improved fertility in women [32] and may also increase the chances of pregnancy and live birth for women undergoing MAR [33]. While there is no specific dietary patterns recommended for women with DOR, markers of ovarian reserve have been shown to be negatively associated with adherence to a typical Western diet [34] (low intakes of fruits and vegetables, high intakes of trans and saturated fats, sugar and sodium). Infertility was less frequent when women were consuming a "fertility" dietary pattern in a large prospective cohort study [35]. The "fertility diet", described as higher intakes of protein from vegetable sources, full-fat dairy foods, iron, mono-unsaturated fatty acids, lower dietary glycaemic index foods and use of multivitamins, was found to have a 66 % lower risk of infertility related to ovulatory disorders and 27 % lower risk of infertility due to other causes compared to women with the lowest intake of this diet pattern [35]. Unexpected poor ovarian response is more frequent in women consuming a low fibre dietary pattern [36]. Lower ovarian reserve has been associated with elevated serum pesticide levels [37] which have also been shown to alter menstrual cycle lengths, reduce fertility, increase time to pregnancy and risk of miscarriage [38]. The

**Table 7**
General consensus on commonly prescribed herbal medicines for women with DOR.

| Herbal medicines most often prescribed (round 1 n = 12) | Clinical scenario # | n (%) | Prescribing frequency (round 2 n = 11) | n (%) |
|---|---|---|---|---|
| *Vitex agnus-castus* (Chaste tree) | 1 | 12 (100.0) | Often/Always | 11 (100.0) |
| | 2 | 9 (75.0) | Sometimes | 0 (0.0) |
| | 3 | 11 (91.7) | Never/Rarely | 0 (0.0) |
| *Withania somnifera* (Withania) | 1 | 10 (83.3) | Often/Always | 11 (100.0) |
| | 2 | 6 (50.0) | Sometimes | 0 (0.0) |
| | 3 | 8 (66.7) | Never/Rarely | 0 (0.0) |
| *Asparagus racemosus* (Shatavari) | 1 | 8 (66.7) | Often/Always | 10 (90.9) |
| | 2 | 7 (58.3) | Sometimes | 1 (9.1) |
| | 3 | 6 (50.0) | Never/Rarely | 0 (0.0) |
| *Paeonia lactiflora* (Peony) | 1 | 6 (50.0) | Often/Always | 8 (72.7) |
| | 2 | 5 (41.7) | Sometimes | 3 (27.3) |
| | 3 | 5 (41.7) | Never/Rarely | 0 (0.0) |
| *Tribulus terrestris (Tribulus)* | 1 | 5 (41.7) | Often/Always | 5 (45.5) |
| | 2 | 3 (25.0) | Sometimes | 5 (45.5) |
| | 3 | 3 (25.0) | Never/Rarely | 1 (9.1) |
| *Angelica polymorpha* (Dong quai) | 1 | 2 (16.7) | Often/Always | 5 (45.5) |
| | 2 | 1 (8.3) | Sometimes | 6 (54.6) |
| | 3 | 0 (0.0) | Never/Rarely | 0 (0.0) |
| *Rehmannia glutinosa* (Rehmannia) | 1 | 2 (16.7) | Often/Always | 5 (45.5) |
| | 2 | 1 (8.3) | Sometimes | 5 (45.5) |
| | 3 | 2 (16.7) | Never/Rarely | 1 (9.1) |
| *Actaea racemosus (Black cohosh)* | 1 | 3 (25.0) | Often/Always | 4 (36.4) |
| | 2 | 2 (16.7) | Sometimes | 5 (45.5) |
| | 3 | 1 (8.3) | Never/Rarely | 2 (18.2) |
| *Glycyrrhiza* spp. (Licorice) | 1 | 2 (16.7) | Often/Always | 2 (18.2) |
| | 2 | 1 (8.3) | Sometimes | 8 (72.7) |
| | 3 | 2 (16.7) | Never/Rarely | 1 (9.1) |
| *Chamaelirium luteum (False unicorn root)* | 1 | 2 (16.7) | Often/Always | 4 (36.4) |
| | 2 | 0 (0.0) | Sometimes | 2 (18.2) |
| | 3 | 1 (8.3) | Never/Rarely | 5 (45.5) |

Clinical scenarios: #1 Trying to conceive (TTC) naturally, #2 TTC with medically assisted reproduction (MAR), #3 Not currently TTC; DOR = diminished ovarian reserve.

main source of human pesticide exposure comes from pesticides in food [39,40].

Experts recommended nutritional supplements including coenzyme Q10 (coQ10), B vitamins, fish oil, zinc, vitamin D and vitamin C for the treatment of women of DOR. Oral supplementation with CoQ10 has the most evidence in favour of its use in the treatment of women with DOR. A small RCT of women with DOR undergoing MAR showed oral supplementation of CoQ10 may increase clinical pregnancy rates, however, there was no effect on live birth or miscarriage rates [41]. Supplementation with antioxidants may theoretically reduce free radical damage to ovarian tissue and oocytes [42], however, the clinical evidence is limited by low quality clinical trials and clinical trial heterogeneity. A recent systematic review of 63 RCTs involving 7760 women attending reproductive clinics taking oral antioxidant supplements (including coQ10, vitamin C, vitamin D and B vitamins) found limited positive effects on live birth rates and clinical pregnancy rates, with no effect on rates of miscarriage [43]. However, the population included women with subfertility, only two studies were specific to women with DOR with no effect on clinical pregnancy rates when comparing antioxidants with placebo (odds ratio (OR) 1.88, 95 % CI 0.86 to 3.37; P = 0.13, $I^{2=}$0 %) [43].

Herbal medicines were reported as being used by the experts when treating women with DOR, with consensus reached for three: *Vitex agnus-castus* (chaste tree), *Withania somnifera* (withania) and *Asparagus racemosus* (shatavari). *V. agnus-castus* has the most research for its use in female reproductive disorders. A small RCT of women with premature ovarian ageing using letrazole with *V. agnus-castus* during the follicular phase compared to letrazole alone demonstrated an increased pregnancy rate [44]. A systematic review reported that small studies suggest benefits of *V. agnus-castus* extracts in the treatment of premenstrual syndrome, premenstrual dysphoric disorder, and latent hyperprolactinaemia [45]. The latter action of the herb is in-line with the expert's intention who reported that they would use *V. agnus-castus* to regulate the menstrual cycle and support luteal phase issues.

*W. somnifera* was recommended by the experts for women with DOR as a general tonic and stress support. *W. somnifera* is a well-known

**Table 8**
General consensus on secondary herbal medicines as part of a formulation for women with DOR.

| Herbal medicines (recommended by one practitioner only) | Importance of the herb as part of a dispensary (round 2 n = 11) | n (%) |
|---|---|---|
| *Zingiber officinale* (Ginger) | Very useful/useful | 6 (54.5) |
| | Sometimes use | 2 (18.2) |
| | Never/Rarely use | 3 (27.3) |
| *Cinnamomum verum* (Cinnamon) | Very useful/useful | 5 (45.5) |
| | Sometimes use | 3 (27.3) |
| | Never/Rarely use | 3 (27.3) |
| *Dioscorea villosa* (Wild yam) | Very useful/useful | 5 (45.5) |
| | Sometimes use | 3 (27.3) |
| | Never/Rarely use | 3 (27.3) |
| *Curcuma longa* (Turmeric) | Very useful/useful | 4 (36.4) |
| | Sometimes use | 3 (27.3) |
| | Never/Rarely use | 4 (36.4) |
| *Ginkgo biloba* (Ginkgo) | Very useful/useful | 4 (36.4) |
| | Sometimes use | 3 (27.3) |
| | Never/Rarely use | 4 (36.4) |
| *Silybum marianum* (St Mary's Thistle) | Very useful/useful | 3 (27.3) |
| | Sometimes use | 2 (18.2) |
| | Never/Rarely use | 6 (54.5) |
| *Urtica dioica folia* (Nettle leaf) | Very useful/useful | 3 (27.3) |
| | Sometimes use | 2 (18.2) |
| | Never/Rarely use | 6 (54.5) |
| *Camellia sinensis* (Green tea) | Very useful/useful | 3 (27.3) |
| | Sometimes use | 1 (9.1) |
| | Never/Rarely use | 7 (63.7) |
| *Codonopsis pilosula* (Codonopsis) | Very useful/useful | 2 (18.2) |
| | Sometimes use | 4 (36.4) |
| | Never/Rarely use | 5 (45.5) |
| *Salvia rosmarinus* (Rosemary) | Very useful/useful | 2 (18.2) |
| | Sometimes use | 4 (36.4) |
| | Never/Rarely use | 5 (45.5) |

DOR = diminished ovarian reserve.

Ayurvedic adaptogen/anti-stress agent that enhances the body's resilience to stress [46]. Significant stress-relieving effects of *W. somnifera* have been demonstrated in a small study of 60 adults [47]. *A. racemosus* was recommended as an ovarian and uterine tonic and for stress support. Animal studies demonstrate increased oestrogen levels, uterine weight and regulation of ovulatory cycles [48]. One small RCT found that A. *racemosus* was comparable to clomiphene citrate in stimulating follicle growth and ovulation in anovulatory women but not as effective for pregnancy rates [49].

### 4.1. Implications

The Delphi method was applied to describe naturopathic management of women with DOR. The Delphi technique is rigorous and given that there was a good response, retention rates (92 % in two rounds), and consensus was reached quickly, we can feel confident in these results. Experts reached consensus on practice behaviours, commonly utilised diets, nutritional supplementation and herbal medicines. Our findings are important because we know that women trying to achieve pregnancy seek naturopathic care [9] but it was not previously known how naturopaths approach treatment. This is an important step in the development of a complex intervention that can be used in a RCT that will investigate the effectiveness of whole-system naturopathy for women with DOR and, therefore, inform clinical practice. The findings may be applicable to any country whose naturopaths practice in a similar way to those in Australia and New Zealand. This is the first study of its type and provides novel insights into the practice behaviours of naturopaths in their treatment of women with DOR.

### 4.2. Limitations

This study has the inherent limitations specific to this design. Although Delphi studies are influenced by researchers, the questionnaires were anonymously completed, thereby minimizing the potential for influence and/or bias. It is possible that despite our best efforts, our recruitment method may have introduced a selection bias in our panel of experts. This choice of recruitment was a practical decision, as there is no registry of naturopaths that practice in women's reproductive health and fertility. All experts were female which is representative of the industry where there tends to be more female naturopaths than males. In Australia, two thirds of naturopaths are female [50] and in a recent worldwide survey of 478 naturopaths from seven world regions, 73 % of respondents identified as female [26]. There is no data to indicate the naturopaths' focus in clinical practice. The results of this Delphi are specific to the way that naturopaths practice in Australia and New Zealand and may not be translatable to naturopathic practices worldwide. We chose to limit the focus to these countries specifically so that the naturopathic intervention would be suitable for a future clinical trial in Australia. Future research should look to reflect on and revise these guidance consensus statements particularly in other geographic and regulatory jurisdictions in the naturopathic profession.

## 5. Conclusion

This Delphi study explored what expert naturopathic practitioners' thought were crucial treatment characteristics and components for managing women with DOR. Consensus was reached for consultation characteristics, topics discussed at consultations, treatment aims, clinical outcomes, dietary patterns, and supplementation of nutrients and herbal medicines. The findings suggest that treatment focuses on promoting well-being and is customised to the individual. This Delphi study constitutes a robust starting point for guiding the development of interventions aiming to improve general well-being and/or fertility in women with DOR trying to conceive naturally or with MAR.

## Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## CRediT authorship contribution statement

**Alison Maunder:** Conceptualization, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. **Susan Arentz:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Mike Armour:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Michael F. Costello:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Carolyn Ee:** Conceptualization, Methodology, Supervision, Writing – review & editing.

## Declaration of competing interest

Authors AM, CE, SA and MA are academic researchers at NICM Health Research Institute. As a medical research institute, NICM Health Research Institute receives research grants and donations from foundations, universities, government agencies, and industry. Sponsors and donors provide untied and tied funding for work to advance the vision and mission of the Institute.

AM declares that she is a naturopathic practitioner at a clinic in Sydney, Australia. She is the recipient of a scholarship from the Jacka Foundation of Natural Therapies for her PhD. The funding body had no role in the design of the study, in the collection, analyses, or interpretation of data, in the writing of the manuscript, or in the decision to publish the results.

CE declares that she is the Jacka Foundation Senior Research Fellow, Chair of the RACGP Integrative Medicine Specific Interest Network (voluntary role), Program Lead of an academic integrative healthcare centre (no financial interest), past General Practitioner Advisory Board member for Blackmores Research Institute, has received industry funding from nutraceutical device companies to conduct clinical trials, and has received honoraria and had travel expenses covered for presenting at complementary medicine events.

SA declares that she is a naturopathic practitioner at an obstetrics and gynaecology clinic in Sydney, Australia. She has received payment for providing expert editing of naturopathic and herbal medicine educational programs, and for investigation of naturopathy, herbal medicines and nutraceuticals in clinical trials and spoken at workshops, seminars and conferences for which registration, travel and/or accommodation has been paid by the organisers.

MA declares that he is the chair of the Research Studies committee and the chair of the Clinical Advisory Committee, both for Endometriosis Australia. He works in private clinical practice as a TEAM practitioner at Sydney Endometriosis. He has received funding from Metagenics, Oz Medicann Group, the Medical Research Futures Fund, Canopy Growth and the Victorian Government, all outside the submitted work.

MC has no competing interests.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctcp.2024.101839.

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