BMJ Open

Effectiveness of an anti-inflammatory diet before in vitro fertilisation in women with endometriosis: protocol for a randomised controlled trial

Paola Viganò ,[1] Martina Abodi,[2,3] Laura Benaglia,[1] Ilaria Bolis,[4] Maira Casalechi,[1] Claudia Ferraro,[1] Letizia Li Piani,[2] Marco Reschini,[1] Fabiana Ruggiero,[1] Noemi Salmeri,[2] Edgardo Somigliana,[1,2] Andrew W Horne ,[5] Annemiek W Nap,[6] Marie-Madeleine Dolmans,[7] EUmetriosis Working Group

To cite: Viganò P, Abodi M, Benaglia L, *et al*. Effectiveness of an anti-inflammatory diet before in vitro fertilisation in women with endometriosis: protocol for a randomised controlled trial. *BMJ Open* 2025;**15**:e108596. doi:10.1136/bmjopen-2025-108596

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2025-108596).

Received 29 July 2025
Accepted 21 November 2025

Check for updates

© Author(s) (or their employer(s)) 2025. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ Group.

For numbered affiliations see end of article.

Correspondence to
Paola Viganò;
paola.vigano@policlinico.mi.it

ABSTRACT

Introduction Endometriosis is a common, benign, chronic inflammatory disease with multiple consequences, from chronic pain to systemic comorbidities and poor quality of life. As it usually affects people of reproductive age, one of the most distressing consequences is infertility, which can be only partly overcome by medically assisted reproduction. Poor outcomes are, in fact, frequent adverse events. As no definitive therapy exists for endometriosis-related infertility, affected women often tend to try either complementary and alternative medicine or self-management strategies to improve their quality of life, with the hope of also enhancing their fertility. Among available options, dietary interventions are commonly explored, even if no robust evidence is available on the optimal type of diet and its effects on reproductive outcomes. This trial will investigate whether an anti-inflammatory dietary intervention can improve fertility outcomes in women affected by endometriosis undergoing in vitro fertilisation (IVF).

Methods and analysis The DietAry interveNtion in ameliorating fertiliTy parameters in women with Endometriosis undergoing IVF (DANTE) study is a single-centre, randomised, controlled, non-pharmacological interventional trial in patients living with endometriosis who are infertile and require IVF. Participants will be allocated to either a 12-week intervention based on an anti-inflammatory diet or no diet before the beginning of controlled ovarian stimulation. Following baseline assessment, 438 participants aged <40 years with a diagnosis of infertility according to WHO criteria (ie, not conceiving after 12 months or more of regular unprotected intercourse) and a normal ovarian reserve will be randomly allocated to one of the two groups (1:1 ratio). In both groups, the dietary habits of participants will be assessed at baseline, and adherence to the intervention will be monitored throughout the study period via 24-hour recalls and food diaries. Participants will provide biological samples (peripheral blood, vaginal swabs and faeces) before and after the intervention to evaluate potential differences in inflammatory markers and microbiome composition between the two groups and across timepoints (before and after diet in the intervention group). Follicular fluid will be collected at the time of oocyte retrieval to describe potential difference in sex steroid levels. Patients will also complete questionnaires on quality of life, sexual function and symptom severity before and after the intervention to assess differences between the two groups and across time points. The primary outcome will be the rate of inadequate ovarian response (defined as the retrieval of ≤3 oocytes according to the Poseidon 2016 criteria) at the time of oocyte retrieval in the treatment versus the no-treatment groups. Secondary outcomes will include clinical pregnancy and live birth rates, IVF-related embryological outcomes, inflammatory marker levels in peripheral blood, vaginal and bowel microbiota features, steroid composition of follicular fluid, life quality and pain symptoms variation.

Ethics and dissemination The study has received ethics approval from Comitato Etico Territoriale Lombardia 3 (#5587_18.12.2024). Results will be presented in peer-reviewed journals and at international conferences.

Trial registration number NCT06885125.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study will be the first randomised controlled trial with sufficient statistical power to establish the impact of an anti-inflammatory diet on reproductive outcomes in women affected by endometriosis.
⇒ The diet was carefully developed by nutritionists and dietary adherence will be closely monitored throughout the study period.
⇒ The study will evaluate both short-term and long-term outcomes and take a comprehensive and multidisciplinary approach by exploring both objective and subjective outcomes, spanning from vaginal microbiome to sexual function.
⇒ The participants cannot be blinded, due to the inherent characteristics of the dietary intervention.
⇒ The context-specific nature of the dietary intervention may reduce the generalisability of the findings, as the control group in Italy may not be comparable to other settings.

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

INTRODUCTION

Endometriosis is a chronic condition estimated to affect approximately 10% of the population assigned female sex at birth, but its true prevalence is likely higher.[1] Despite having a frequency comparable to other common conditions, such as diabetes or Crohn's disease, endometriosis remains one of the most under-researched and underfunded diseases worldwide.[2] This disparity has contributed to significant diagnostic delays, limited treatment options and a general lack of personalised evidence-based care.[3 4]

Together with pelvic pain, infertility is one of the most distressing consequences of endometriosis, as it affects individuals of reproductive age, thereby representing a significant global health concern.[5 6] Inflammation plays a central role in the pathophysiology of both pain and infertility associated with the disease, contributing to the establishment and maintenance of lesions, as well as to the associated symptoms.[7–9] Inflammatory mediators activate peripheral nociceptors, exacerbating chronic pelvic pain and promoting sensitisation.[10] The persistent inflammatory milieu is also detrimental to fertility as it impairs folliculogenesis and compromises gamete function and fertilisation.[11 12]

Managing endometriosis-related infertility remains a clinical challenge. Although surgical treatment of superficial peritoneal endometriosis has shown some benefits,[13] the effectiveness of surgery has been increasingly questioned in the case of ovarian endometriosis, due to its potential negative impact on ovarian reserve.[14 15] Medically assisted reproduction is frequently proposed as an alternative[11]; however, the decision between in vitro fertilisation (IVF) and surgery continues to be debated.[16] Importantly, IVF outcomes in individuals with endometriosis are often suboptimal, with lower oocyte yields and reduced pregnancy rates compared with other populations experiencing infertility.[17 18] These limitations have fuelled growing interest in identifying non-invasive, adjunctive strategies aimed at improving IVF outcomes in subjects with endometriosis. Notably, many affected individuals turn to lifestyle modifications and complementary and alternative medicine, such as acupuncture, dietary interventions and physical activity, to self-manage their symptoms and the consequences of the disease.[19 20]

The role of diet

Among emerging self-management strategies for endometriosis, dietary modifications have garnered growing attention,[21] as they represent one of the most accessible self-management measures. As a modifiable factor of everyday life, diet influences systemic inflammation, hormonal regulation, immune system, microbiome composition and general health,[22–24] positioning it as a potentially accessible and cost-effective component of endometriosis management. Although no specific diet for endometriosis can be supported considering available evidence, it is clear how, rather than focusing on single nutrients, investigating overall dietary patterns provides a more holistic understanding of the relationship between nutrition and the disease.[25 26]

In a prospective cohort study conducted in 2024, dietary habits were evaluated in relation to the risk of an endometriosis diagnosis in a population of 81,997 reproductive-aged women.[27] A 27% higher risk of being diagnosed with endometriosis was observed in women with dietary patterns characterised by a higher intake of red and processed meat, refined grains and sweets—typical of the Western dietary pattern. A cross-sectional study based on the National Health and Nutrition Examination Survey including 265 women with self-reported endometriosis found that those in the highest tertile of the Dietary Inflammatory Index (DII), a validated tool to quantify dietary inflammatory potential, had a significantly higher risk of endometriosis (OR: 1.57; 95% CI 1.14 to 2.17; p=0.007), supporting a positive association between pro-inflammatory diets and endometriosis risk.[28]

Further clarity is needed to understand the underlying mechanisms through which dietary interventions may exert beneficial effects in endometriosis. However, given the biological nature of the disease, it is reasonable to believe that these benefits are likely primarily related to the anti-inflammatory effects of the intervention and its potential to reduce oestrogen levels.[29] The Mediterranean diet, characterised by a high intake of anti-inflammatory components such as fruits, vegetables, legumes, whole grains, fish rich in omega-3 fatty acids and olive oil, has shown promise in small-scale trials. A 6-month intervention based on the Mediterranean dietary pattern improved metabolic and oxidative profiles and enhanced quality of life in patients with endometriosis.[30]

Study aim

The DietAry interveNtion in ameliorating fertiliTy parameters in women with Endometriosis (DANTE) randomised controlled trial (RCT) aims to compare reproductive outcomes in infertile patients with endometriosis undergoing a standard IVF protocol after a 12-week intervention based on an anti-inflammatory diet versus a standard IVF protocol. Specifically, the primary endpoint will be the rate of poor ovarian response, defined according to the POSEIDON criteria (2016)[31] as the retrieval of ≤3 oocytes during IVF.

Secondary endpoints will address the broader impact of the dietary intervention on several clinical, biological and patient-reported outcome measures (PROMs), including:

- Changes in systemic inflammation as reflected by the low-grade INFLAmmation Score (INFLA)[32 33] (measured at baseline and end of study in both groups).
- Changes in composition and diversity of the faecal and vaginal microbiome (measured at baseline and end of study in both groups).
- Changes in quality of life assessed using the Endometriosis Health Profile-30 (EHP-30[34]; measured at baseline and end of study in both groups).
- Changes in symptom severity, measured through the Numeric Rating Scale (NRS)[35] specifically

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

addressing multiple endometriosis-specific pain domains: dysmenorrhoea, superficial dyspareunia, deep dyspareunia, dyschezia and dysuria (measured at baseline and end of study in both groups).
- Changes in sexual function, evaluated using the Female Sexual Function Index (FSFI[36]; measured at baseline and end of study in both groups).
- Differences between the intervention and control groups in concentrations of steroid hormones in the follicular fluid to explore effects of the diet on the local hormonal environment.[37]
- Differences between the intervention and control groups in embryological outcomes, including number of oocytes retrieved, number of cleavage stage embryos and number of blastocysts.[38]
- Differences between the intervention and control groups in pregnancy outcomes, including live birth rate, clinical pregnancy rate and miscarriage rate.[38]

We hypothesise that the anti-inflammatory diet will improve oocyte yield, enhance pregnancy and live birth rates, and improve quality of life and sexual function, while reducing symptom severity compared with standard care.

The EUmetriosis project

The DANTE RCT is embedded within the EUmetriosis project, a European Union (EU)-funded initiative under the HORIZON-HLTH-2024-DISEASE-03-two-stage call. The project seeks to address critical knowledge gaps in the pathogenesis, diagnosis and management of endometriosis. Through multiple work packages, it promotes personalised, patient-centred care by supporting self-management strategies and the development of non-invasive, accessible treatments.

METHODS AND ANALYSIS

Study design

This protocol (V.1.0) outlines a two-arm, parallel-group, assessor-blinded, superiority RCT. The study will be reported in accordance with the Standard Protocol Items: Recommendations for Interventional Trials guidelines and Consolidated Standards of Reporting Trials statement.[39 40] The study will be conducted at the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. Randomisation will last from March 2025 to January 2029. The primary endpoint will be assessed at the time of oocyte retrieval, approximately 14 weeks after randomisation. The study is registered on ClinicalTrials.gov (NCT06885125; 20.03.2025). The WHO Trial Registration Data Set is shown in online supplemental table 1.

Participants

The study will enrol 438 infertile subjects with endometriosis aged 18–39 years. The definition of infertility will follow WHO criteria (ie, not conceiving after 12 months or more of regular unprotected intercourse). The diagnosis of endometriosis for eligibility will be based either on surgical reports with histological confirmation of the disease or on imaging for endometrioma or deep endometriosis, according to international standards. All the inclusion and exclusion criteria are reported in table 1.

Table 1 Eligibility criteria

Inclusion criteria	Exclusion criteria
Age 18–39 years	Contraindication to pregnancy
Pregnancy seeking for more than 12 months	Hydrosalpinx
Regular menstrual cycle (21–35 days)	Endometriomas with mean diameter >4 cm
Normal ovarian reserve (AFC ≥5); signed informed consent form	Severe male factor (<1 million sperm/mL); SM fibroids or large IM/SS fibroids (≥5 cm)
	Doubtful US findings that do not allow to reliably rule out malignancies
	Ureteral stenosis or intestinal subocclusive symptoms

AFC, antral follicular count; IM, intramural; SM, submucosal; SS, subserosal; US, ultrasound.

Recruitment and screening procedure

Figure 1 shows the flowchart of the RCT. At their first routine consultation in our IVF unit (T-1), individuals affected by endometriosis will undergo screening which includes the comprehensive transvaginal ultrasound examination to confirm the presence of endometriosis. Eligible participants will receive detailed information by the study team about the study purpose, procedures, temporal commitment, possible discomforts and potential risks and benefits. Participation will be entirely voluntary, with the right to withdraw at any time. Finally, a written informed consent form will be obtained from all participants willing to participate. Patient consent form can be found in the online supplemental material.

Randomisation procedure, concealment of allocation and blinding

The second consultation (T0) will be scheduled on days 5–7 of the menstrual cycle. For participants with menstrual suppression due to continuous hormone therapies, the timing of the cycle will not be considered. Baseline and clinical data will be collected during a gynaecological visit, and a nutritional assessment will be conducted. After the initial gynaecological and nutritional visits, patients will be randomly assigned (1:1 ratio) to either:
- a control group receiving no specific dietary instructions, or
- an anti-inflammatory dietary intervention group.

Randomisation will be conducted via the secure Research Electronic Data Capture (REDCap; Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico Milano version: https://redcap.policlinico.mi.it/; Vanderbilt University, Nashville, TN, USA), using a

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

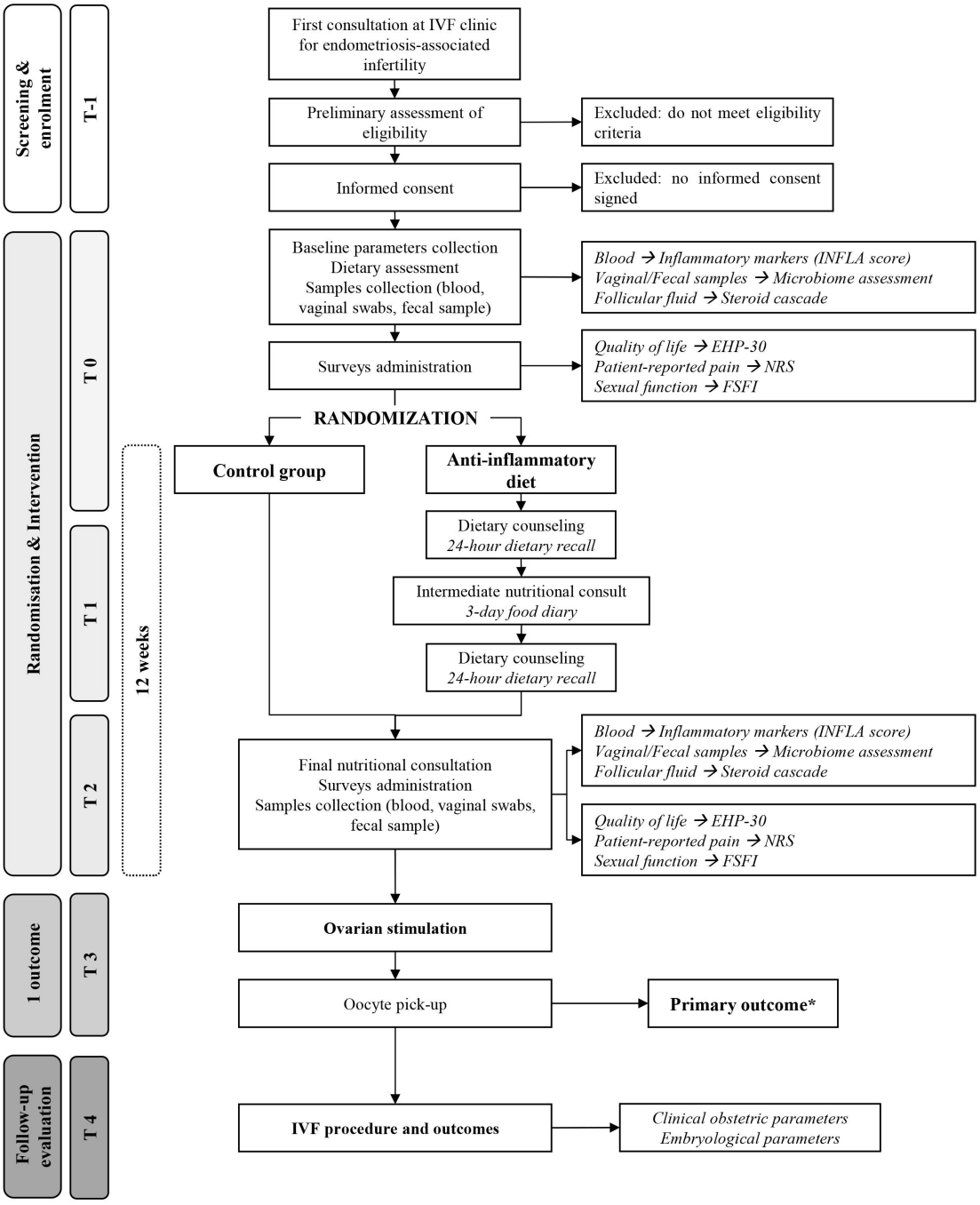

Figure 1 Standard Protocol Items: Recommendations for Interventional Trials 2025. Diagram of the schedule of enrolment, interventions and assessments. *According to Poseidon criteria (difference in the proportion of women with less than 4 oocytes at oocyte retrieval). EHP-30, Endometriosis Health Profile-30; FSFI, Female Sexual Function Index; INFLA, low-grade INFLAmmation score; IVF, in vitro fertilisation; NRS, Numeric Rating Scale.

computer-generated allocation sequence and block randomisation to ensure balance and conceal allocation. The block size will remain undisclosed to participants and investigators. Allocation will be revealed automatically at the time of randomisation for each individual participant. Blinding will be maintained for both the clinical and lab staff performing the ovarian stimulation and IVF lab procedures, respectively. An independent external monitor will oversee study progress and ensure compliance with data management protocols.

Gynaecological assessment

A detailed clinical gynaecological assessment will be performed according to internationally recognised standards, following the evaluation criteria established by the World Endometriosis Society and the World Endometriosis Research Foundation.[41] The assessment will include a thorough pelvic examination and structured symptom evaluation. Imaging will be conducted using high-resolution transvaginal ultrasound, performed in accordance with the International Deep Endometriosis

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Analysis consensus statement[42] to ensure standardised and reproducible mapping of endometriosis-related deep lesions. Pain severity will be recorded using the NRS for endometriosis-specific pain domains, including dysmenorrhoea, superficial and deep dyspareunia, dyschezia and dysuria.

Nutritional assessment

At T0, the nutritional status will be assessed by a clinical nutritionist through the evaluation of dietary habits, gastrointestinal (GI) symptoms, physical activity, anthropometric parameters and body composition. Anthropometric measurements will be repeated at week 6 of the intervention for the intervention group and at week 12 for both intervention and control groups.

Dietary habits of the 6 months before the enrolment will be investigated through a 78-item Food Frequency Questionnaire, validated for the Italian population.[43] The dietary inflammatory potential for each participant will be assessed by calculating the DII score, which provides a negative score to nutrients such as magnesium, vitamins A, C, D and E, flavonoids, fibre, monounsaturated and polyunsaturated fatty acids, tea, garlic and ginger (anti-inflammatory), and a positive score to pro-inflammatory components as cholesterol, saturated fats, refined carbohydrates, total protein, vitamin B12 and high caloric intake.[44 45]

Anthropometric measures of height, weight and circumferences (chest, breast, arm, wrist, waist, abdomen, hip, thigh, knee and ankle) will be assessed according to standard procedures, using appropriate instruments (an electronic scale with 100 g precision, a stadiometer with 1 mm precision and a non-elastic measuring tape with 1 mm precision; doi.org/10.1249/00005768-199208000-00020). Body composition will be estimated through bioelectrical impedance analysis with Akern 101 BIVA pro (Akern Bioresearch, Florence, Italy), measuring resistance, reactance and phase angle parameters following the guidelines of the European Society of Parenteral and Enteral Nutrition.[46 47]

Interventions

The anti-inflammatory dietary intervention and standard care dietary are summarised aligning to Template for Intervention Description and Replication guidelines[48] (table 2).

Control group

After randomisation, no specific dietary guidance or recommendations will be provided to participants allocated to the control group, allowing them to maintain their habitual eating patterns. They will begin the standard IVF treatment protocol no earlier than 12 weeks after the initial visits.

Anti-inflammatory dietary intervention group

Participants will be encouraged to follow an anti-inflammatory dietary intervention based on the Mediterranean diet principles. The anti-inflammatory potential of the diet will be assessed by calculating the DII score. The consultation will include a comprehensive explanation of the anti-inflammatory dietary principles, the rationale behind the intervention, the potential benefits and risks, and a space to address participant concerns. Participants in the dietary intervention group will receive a general guide along with the personalised meal plan for 3 weeks to repeat throughout the intervention period. Nutritional advice will include the use of extra virgin olive oil as the main cooking fat (at least 4 tablespoons/day), consumption of whole grains, nuts, at least 2 servings of fresh and seasonal fruit per day, at least 2 servings of fresh and seasonal vegetables per day, at least 2 servings of fish per week (especially varieties rich in omega-3), no more than 2 servings of red meat per month, consumption of organic foods, and the use of anti-inflammatory spices such as ginger, garlic and curcumin and avoidance of ultra-processed foods such as pre-cooked meals, breakfast cereals, biscuits, pre-sliced bread, rusks, sweetened beverages with added sugars, salt, refined oils, trans fats or food additives. Recommendations will be personalised based on energy needs (estimated according to the Nutrient and Energy Reference Values for the Italian Population (LARN V Revision; https://eng.sinu.it/larn)) and calculation of ideal weight,[49] intestinal symptoms, body composition, and dietary preferences and allergies.

To monitor dietary adherence, a 24-hour dietary recall will be conducted via telephone at both 3 and 9 weeks following the baseline visit (T0). At 6 weeks, participants in the intervention group will attend a second in-person consultation with the nutritionist who will further evaluate adherence with a 3-day food diary and measure anthropometric parameters. Patients in the control group will undergo the same final nutritional evaluation with a 3-day food diary to confirm that no consistent change in dietary habits and inflammatory potential occurred. The dietary intervention will span the 12 weeks leading up to the beginning of the ovarian stimulation (between T0 and T2) when a final in-person consultation will take place. Participants will be encouraged to follow the dietary advice until, at least, oocyte pick-up (T3; figure 1).

Data and specimen collection and lab analysis

Clinical, biological and nutritional data will be collected at multiple timepoints (table 3). All data will be collected using the REDCap platform.

At baseline (T0), all participants will be asked to provide biological samples, including a peripheral blood sample, vaginal swabs and faeces. The same collection will be repeated at the end of the 12-week intervention period, prior to the initiation of the ovarian stimulation (T2). To minimise differences due to the menstrual cycle, all samples will be collected between day 5–7 of the menstrual cycle, or for participants with menstrual suppression due to continuous hormone therapies before IVF, without taking the cycle timing into consideration.

The biological samples will be analysed as follows:

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 2 Overview of intervention delivery described according to the TIDieR guidelines

Brief name	Anti-inflammatory dietary programme	Standard care
Why	Anti-inflammatory diets targeting systemic inflammation assist in the prevention and management of various chronic diseases and chronic pain conditions; inflammation is also supposed to play a pivotal role in endometriosis natural history and in infertility occurrence	
What (materials)	Participants will receive an intervention handbook containing all study details, key anti-inflammatory eating principles, meal plans, frequently asked questions, foods encouraged and discouraged, and education (eg, common myths, tips for eating out and shopping tips); and a specific meal guide personalised for the patient according to previous consultation, allergies and preferences	
What (procedures)	Participants are encouraged to follow an anti-inflammatory dietary intervention based on Mediterranean diet principles. The consultation will include a comprehensive explanation of the anti-inflammatory dietary principles, the rationale behind the intervention, the potential benefits and risks, and a space to address participant concerns; a 24-hour dietary recall will be conducted via telephone at both 3 and 9 weeks to monitor dietary adherence; participants will attend a second in-person consultation with the nutritionist at 6 weeks, who will further evaluate adherence with a 3-day food diary and assess anthropometric parameters; the dietary intervention will span 12 weeks leading up to the beginning of the ovarian stimulation, when a final in-person consultation will take place and anthropometric parameters will be reassessed	At the end of the 12-week period, participants will attend a single consultation with the nutritionist to assess anthropometric and dietary parameters
Who provided	A qualified nutritionist specially trained to deliver all components	A qualified nutritionist specially trained to deliver all components
How	Delivered with individual support for 12 weeks; consultations are one-to-one, in person or by phone	
Where	In-person consultations will occur at Fondazione Ca' Granda, Milan; additional consultations will occur via telephone; participants will integrate the diet principles into their daily consumption of foods and beverages	In-person consultations will occur at Fondazione Ca' Granda, Milan
When and how much	Three in-person consultations at baseline, week 6 and week 12; two phone follow-up consultations (~30 min) at weeks 3 and 9	Two in-person consultations at baseline and week 12
Tailoring	Anti-inflammatory dietary advice, education and support aligning with participant preferences and goals	
Modifications	Any modifications will be reported	Any modifications will be reported
How well (planned)	Clinical nutritionists receive prior training to standardise measurements and unify information delivered in the programme; participant adherence to the anti-inflammatory diet is assessed through 24-hour recall and 3-day food diaries	Clinical nutritionists receive prior training to standardise measurements and unify information delivered in the programme
How well (actual)	Reported in the primary paper	

TIDieR, Template for Intervention Description and Replication.

- Peripheral blood samples will be analysed for systemic inflammation using the INFLA-score, which summarises the synergistic effects of C-reactive protein levels, white blood cell count, platelet count and the granulocyte-to-lymphocyte ratio.[50]
- Vaginal swabs and faecal samples will be investigated for bacterial abundance and diversity by microbiome analysis at the University College Cork – National University of Ireland in Cork. These samples will be processed for bacterial DNA extraction and analysed using high-throughput amplicon sequencing targeting the *16S rRNA* gene. Sequencing will be performed, followed by comprehensive bioinformatics processing to characterise the microbial communities.[51]
- Follicular fluids will be analysed for sex steroids concentrations quantified using liquid chromatography–tandem mass spectrometry. Hormones to be measured include aldosterone, androstenedione, cortisol, corticosterone, 11-deoxycorticosterone, 11-deoxycortisol, 21-deoxycortisol, dehydroepiandrosterone (DHEA), DHEA sulphate, dihydrotestosterone, estradiol, 17-OH progesterone, progesterone and testosterone.[37]

Outcome measures

Primary outcome

The primary outcome is the difference in the rate of poor ovarian responders despite preserved ovarian reserve

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 3 Overview of data collection

Variable	T0	T1	T2	T3	T4
Participant characteristics					
Age (years)	x				
FSH (IU/mL)	x				
AMH (ng/mL)	x				
AFC	x				
Duration of infertility (ms)	x				
Previous deliveries	x				
Smoking	x				
Medical history, comorbidities	x				
Anthropometric parameters					
Height, weight and waist circumference	x		x		
Body composition	x		x		
BMI (kg/m^2)	x		x		
Treatment and IVF results					
Ovarian stimulation protocol				x	
Total dose of gonadotrophins used (IU)				x	
Days of COH				x	
Number of oocytes				x	
Number of MII oocytes				x	
Fertilisation rate (%)					x
Number of embryos at 72 hours					x
Number of blastocysts					x
Biological samples					
Blood	x		x		
Faecal sample	x		x		
Vaginal swabs	x		x		
Follicular fluid				x	
Dietary assessment					
Food frequency questionnaire	x		x		
DII score	x		x		
24-hour recall		x			
3-day diary		x	x		
Obstetric outcomes					
Pregnancy					x
Miscarriages					x
Delivery					x
Newborn outcome					x
Pregnancy complications					x
Patient-reported outcomes					
SF-12	x		x		
EHP-30	x		x		
NRS	x		x		
Medication use	x	x	x	x	x
Adverse events		x	x	x	x

AFC, antral follicular count; AMH, anti-Müllerian hormone; BMI, body mass index; COH, controlled ovarian hyperstimulation; DII, Dietary Inflammatory Index; EHP-30, Endometriosis Health Profile-30; FSH, follicle-stimulating hormone; IVF, in vitro fertilisation; MII, metaphase II; ms, months; NRS, Numeric Rating Scale; SF-12, Short Form-12.

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

(defined as patients retrieving three or fewer oocytes following controlled ovarian stimulation, according to the Poseidon criteria[31]) between the two arms. The primary outcome will be assessed at the time of oocyte retrieval (T3).

Secondary outcomes

Inflammatory markers

Changes in systemic inflammatory status, as measured by the INFLA-score, will be compared between groups and before and after the intervention, to evaluate the impact of the dietary intervention on the systemic inflammatory profile. This secondary outcome will be assessed on biological samples collected at T0 and T2.

Vaginal and faecal microbiome

The composition and diversity of vaginal and faecal microbiota will be compared between groups, and before and after the intervention. Bioinformatic analyses will allow for detailed evaluation of bacterial abundance and diversity, with subsequent correlation analyses to explore the potential influence of diet on intestinal and vaginal microbiomes and in relation to IVF outcomes. This secondary outcome will be assessed on biological samples collected at T0 and T2.

Patient-reported outcome parameters

PROMs will be evaluated through both between-groups comparisons and within-group changes in the treatment arm after the dietary intervention. Quality of life will be assessed using the EHP-30, the symptom severity using the NRS and the female sexual health using the FSFI. These secondary outcomes will be assessed on questionnaires collected at T0 and T2.

Steroid cascade in the follicular fluid

Changes in the sex steroid hormones in follicular fluid will be compared between groups to evaluate the impact of the dietary intervention on the hormonal milieu. This secondary outcome will be assessed on follicular fluid collected at the time of oocyte retrieval (T3).

Embryological parameters

Embryological outcomes will include the number of mature oocytes (metaphase II (MII)) at the time of oocyte retrieval (T3). Additionally, differences in the number of available embryos and blastocysts will be evaluated between the groups at the follow-up stage (T4).

Pregnancy outcomes

Pregnancy outcomes will include comparison between the two groups regarding live birth, clinical pregnancy and miscarriage rate at the follow-up time (T4).

Data management

Data will be collected and managed electronically using REDCap. Each patient will be assigned a unique code to de-identify their data, ensuring that only local investigators can link the data back to individual identities. The use of REDCap will ensure: (a) user-level access control with specific permissions based on the role of each team member; (b) real-time data validation and integrity check; (c) de-identification of patient information prior to data export; and (d) centralised data storage on a secure server with daily backup to ensure data safety.

Sample size calculation

This trial is powered to detect a clinically significant difference between groups for the primary outcome. A total of 438 women with endometriosis will be randomised to either a control group or an anti-inflammatory dietary intervention group. The sample size calculation is based on the following assumptions: (1) type I and type II errors of 0.05 and 0.20, respectively; (2) an expected rate of poor ovarian response of 20% in the untreated group[38]; (3) an absolute reduction of 10% in poor ovarian response in the dietary intervention group; (4) an estimated drop-out rate due to the withdrawal from the study of 10% from the dietary intervention group, as reported by Zheng *et al*[52]; and (5) use of a two-tailed test for proportions in two independent groups with binomial approximation to the Gaussian distribution (https://www.stat.ubc.ca/~rollin/stats/ssize/b2.html).

Statistical analyses

Statistical analyses will be conducted using IBM SPSS Statistics V.27 (IBM Corp, Armonk, NY, USA). Drop-out of participants for discontinuation of treatment from the dietary intervention group is anticipated; however, as long as ovarian stimulation will start after the intervention period, these participants will not be excluded from the analysis. Therefore, the primary analysis will be done considering the intention-to-treat and a per-protocol (PP) analysis will be conducted to assess the robustness of the findings. The primary outcome will be presented as a percentage in each group, with relative risks and 95% CIs. Differences between the groups will be assessed with the χ^2 test. For secondary outcomes, categorical variables will be compared using χ^2 test or Fisher Exact test, while normally distributed variables will be compared using Student's t-tests. For continuous variables that are not normally distributed, non-parametric tests such as Wilcoxon and Mann-Whitney U tests will be used. IVF and pregnancy outcomes will be reported and analysed following the core outcome set for infertility studies.[53]

ETHICS AND DISSEMINATION

The study protocol was approved by the Ethical Committee (Comitato Etico Territoriale Lombardia 3 - #5587_18.12.2024) on 18 December 2024. The study will be conducted according to the International Council for Harmonisation – Good Clinical Practice guidelines and all applicable regulatory requirements, including the Declaration of Helsinki (June 1964, as revised by the World Medical Association General Assembly in Seoul,

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

2008). All participants will be required to sign a written informed consent prior to enrolment.

Adverse events related to dietary intervention are considered highly unlikely, as the proposed anti-inflammatory diet intervention is composed of foods commonly consumed within the local population. Moreover, the meal plan will be tailored to each participant, taking into account existing food allergies or intolerances. The study imposes no additional medical risk, as all participants would undergo IVF procedures irrespective of study participation. On the contrary, participation in the anti-inflammatory diet arm may offer potential health benefits.

The findings from this study will be disseminated broadly through peer-reviewed scientific journals and presentations at national and international conferences. Only anonymised, aggregated data will be reported. Any significant amendments to the study protocol will be promptly submitted to the responsible ethics committee for approval.

DISCUSSION

This RCT represents the first large-scale study to rigorously evaluate the impact of an anti-inflammatory dietary intervention on reproductive outcomes in subjects with endometriosis. The anti-inflammatory potential of the diet will be quantitatively assessed using the validated DII to ensure therapeutic and biological relevance. By adopting a multidimensional approach, the study not only targets clinical endpoints, such as oocyte yield and live birth rate, but also evaluates critical aspects of patient well-being, including symptom burden, sexual function and overall quality of life.

Given the nature of the intervention, participant blinding is inherently unfeasible; however, outcome assessors will remain blinded to allocation, thereby minimising detection bias. The potential for selection bias is also acknowledged, as participants who opt into a dietary intervention trial may exhibit health-conscious behaviours or motivations not fully representative of the broader endometriosis population. Nonetheless, the robust design of this trial, adequate statistical power and comprehensive outcome set ensure the reliability and translational value of the findings.

Importantly, this study is embedded within the broader framework of EUmetriosis, an international, EU-funded initiative designed to address persistent challenges in the diagnosis and management of endometriosis (https://eumetriosis.eu). The integrative, patient-centred strategy of the project leverages state-of-the-art advances in immunology, microbiome research, metabolomics and epigenetics as well as social science research and patient representative involvement, to enable the development of minimally invasive, personalised therapeutic pathways that are feasible for people to implement and supported by policy contexts. Within this context, our trial contributes uniquely by exploring nutritional modulation as a low-risk, cost-effective and potentially synergistic adjunct to conventional fertility treatments. This intervention could pave the way for non-pharmacological strategies that not only enhance reproductive outcomes but also improve quality of life and reduce the systemic inflammation that characterises endometriosis. The results could help inform future dietary guidelines, patient counselling and integrated care models for women undergoing fertility treatments in the setting of endometriosis.

Author affiliations
[1]Infertility Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[2]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy
[3]ONFoods – Research and Innovation Network on Food and Nutrition Sustainability, University of Milan, Milan, Italy
[4]University of Milan, Milan, Italy
[5]The University of Edinburgh MRC Centre for Reproductive Health, Edinburgh, UK
[6]Obstetrics and Gynaecology, Radboud University Medical Center, Nijmegen, The Netherlands
[7]Department of Gynaecology, Université Catholique de Louvain, Louvain-la-Neuve, Belgium

Acknowledgements MA is thankful to the ONFoods Foundation – Research and Innovation Network on food and nutrition Sustainability, Safety and Security – Working ON Foods.

Collaborators EUmetriosis Working Group: Chloé Beaussart, Paula Blancarte Jaber, Emma Cox, Julie Candiracci, Christophe Depoix, Marie-Madeleine Dolmans, Andrea Ford, Douglas Gibson, Marek Gogacz, Marielle Herzog, Andrew W. Horne, Emma Huijs, Femke Jansen, Maddalena Karadza, Annemiek W Nap, Siobhain O'Mahony, Erica Selznick, Wiktoria Skiba, Loutje van der Sman, Dorota Suszczyk, Athanasios Tsanas, Paola Viganò, Iwona Wertel, Inga Winkler, Ana Zakosek Finka.

Contributors PV, AWN, MMD and AWH conceptualised the trial and obtained funding. PV, MR and NS designed the study protocol with input from MA, LB and IB. MR provided statistical expertise and will conduct primary statistical analysis. MC provided blood analysis expertise and will lead inflammatory marker analyses. LLP drafted the manuscript with input from PV, CF, ES and FR. PV is the guarantor of the study. All authors read and approved the final manuscript.

Funding This work is part of the EUmetriosis project, which is supported by the HORIZON-HLTH-2024-DISEASE-03-two-stage (Tackling diseases (Two stage - 2024)) Proposal number: 101157146-2.

Competing interests PV is co-Editor-in-Chief of the Journal of Endometriosis and Uterine Disorders and declares receiving honoraria for lectures from Gedeon Richter. ES declares receiving honoraria for lectures at meetings from IBSA. He also handles private grants of research from Ferring, IBSA, Theramex and Gedeon Richter, and is Editor-in-Chief of Human Reproduction Open. AWH declares grant funding from UK Research and Innovation, National Institute for Health and Care Research, Chief Scientist Office – Scotland, Wellbeing of Women, Roche Diagnostics and payment to his institution for consultancy from Roche Diagnostics, Gesynta and Joii. AWH has received payment for a lecture from Theramex and Gedeon Richter. MMD declares receiving grants and support for attending meetings from Theramex. All the other authors do not have any conflict of interest to declare.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines,

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: https://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs
Paola Viganò https://orcid.org/0000-0003-3674-5912
Andrew W Horne https://orcid.org/0000-0002-9656-493X

REFERENCES

1 Horne AW, Missmer SA. Pathophysiology, diagnosis, and management of endometriosis. *BMJ* 2022;379:e070750.
2 Viganò P, Casalechi M, Dolmans M-M. European Union underinvestment in endometriosis research. *J Endometr Uter Dis* 2024;5:100058.
3 Al-Lami RA, Taha SA, Jalloul RJ, *et al*. Women with endometriosis in the United States: National Survey of Family Growth, 2011–2019. *J Endometr Uter Dis* 2024;8:100081.
4 As-Sanie S, Black R, Giudice LC, *et al*. Assessing research gaps and unmet needs in endometriosis. *Am J Obstet Gynecol* 2019;221:86–94.
5 Bonavina G, Taylor HS. Endometriosis-associated infertility: From pathophysiology to tailored treatment. *Front Endocrinol (Lausanne)* 2022;13:1020827.
6 Ata B, Somigliana E. Endometriosis, staging, infertility and assisted reproductive technology: time for a rethink. *Reprod Biomed* 2024;49:103943.
7 Dymanowska-Dyjak I, Terpiłowska B, Morawska-Michalska I, *et al*. Immune Dysregulation in Endometriomas: Implications for Inflammation. *IJMS* 2024;25:4802.
8 Donnez J, Dolmans MM. Endometriosis: from iron and macrophages to exosomes. Is the sky clearing? *Hum Reprod Open* 2024;2024:hoae034.
9 Giacomini E, Minetto S, Li Piani L, *et al*. Genetics and Inflammation in Endometriosis: Improving Knowledge for Development of New Pharmacological Strategies. *Int J Mol Sci* 2021;22:9033.
10 Chen Y, Li T. Unveiling the Mechanisms of Pain in Endometriosis: Comprehensive Analysis of Inflammatory Sensitization and Therapeutic Potential. *IJMS* 2025;26:1770.
11 Somigliana E, Li Piani L, Paffoni A, *et al*. Endometriosis and IVF treatment outcomes: unpacking the process. *Reprod Biol Endocrinol* 2023;21:107.
12 Casalechi M, Di Stefano G, Fornelli G, *et al*. Impact of endometriosis on the ovarian follicles. *Best Pract Res Clin Obstet Gynaecol* 2024;92:102430.
13 Bafort C, Beebeejaun Y, Tomassetti C, *et al*. Laparoscopic surgery for endometriosis. *Cochrane Database Syst Rev* 2020;10:CD011031.
14 Garcia-Velasco JA, Viganò P, Somigliana E. Twenty-five years of research in endometriosis. *Reprod Biomed* 2025;50:104830.
15 Invernici D, Fornelli G, Reschini M, *et al*. Ovarian damage following surgery for endometriomas, 20 years later: did awareness improve the situation? *Arch Gynecol Obstet* 2025;312:595–601.
16 Ottolina J, Vignali M, Papaleo E, *et al*. Surgery versus IVF for the treatment of infertility associated to ovarian and deep endometriosis (SVIDOE: Surgery Versus IVF for Deep and Ovarian Endometriosis). Clinical protocol for a multicenter randomized controlled trial. *PLoS One* 2022;17:e0271173.
17 Paffoni A, Casalechi M, De Ziegler D, *et al*. Live Birth After Oocyte Donation In Vitro Fertilization Cycles in Women With Endometriosis: A Systematic Review and Meta-Analysis. *JAMA Netw Open* 2024;7:e2354249.
18 Bourdon M, Peigné M, Maignien C, *et al*. Impact of Endometriosis Surgery on In Vitro Fertilization/Intracytoplasmic Sperm Injection Outcomes: a Systematic Review and Meta-analysis. *Reprod Sci* 2024;31:1431–55.
19 van Haaps AP, Wijbers JV, Schreurs AMF, *et al*. The effect of dietary interventions on pain and quality of life in women diagnosed with endometriosis: a prospective study with control group. *Hum Reprod* 2023;38:2433–46.
20 Su Y, Ji R, Zheng X, *et al*. Efficacy and safety of acupuncture-related therapies in symptomatic endometriosis: a systematic review and network meta-analysis. *Arch Gynecol Obstet* 2025;311:697–714.
21 Salmeri N, Ragusi A, Buffo C, *et al*. Dietary Supplements for Endometriosis-Associated Pain: A Systematic Review and Meta-Analysis of Randomized Placebo-Controlled Trials. *Gynecol Obstet Invest* 2025;2025:1–14.
22 Sowers MR, Crawford S, McConnell DS, *et al*. Selected diet and lifestyle factors are associated with estrogen metabolites in a multiracial/ethnic population of women. *J Nutr* 2006;136:1588–95.
23 Malesza IJ, Malesza M, Walkowiak J, *et al*. High-Fat, Western-Style Diet, Systemic Inflammation, and Gut Microbiota: A Narrative Review. *Cells* 2021;10:3164.
24 Rattan SIS, Kaur G. Nutrition, Food and Diet in Health and Longevity: We Eat What We Are. *Nutrients* 2022;14:5376.
25 Ruotolo A, Vannuccini S, Capezzuoli T, *et al*. Diet characteristics in patients with endometriosis. *J Endomet Uter Dis* 2025;9:100094.
26 Türkoğlu İ, Sacinti KG, Panattoni A, *et al*. Eating for Optimization: Unraveling the Dietary Patterns and Nutritional Strategies in Endometriosis Management. *Nutr Rev* 2025;83:869–79.
27 Dougan MM, Fest S, Cushing-Haugen K, *et al*. A prospective study of dietary patterns and the incidence of endometriosis diagnosis. *Am J Obstet Gynecol* 2024;231:443.
28 Liu P, Maharjan R, Wang Y, *et al*. Association between dietary inflammatory index and risk of endometriosis: A population-based analysis. *Front Nutr* 2023;10:1077915.
29 Huijs E, van Stigt BJ, de Roos N, *et al*. The feasibility of an anti-inflammatory diet in endometriosis: barriers and facilitators perceived by endometriosis patients. *Reprod Biomed* 2024;48:103624.
30 Cirillo M, Argento FR, Attanasio M, *et al*. Atherosclerosis and Endometriosis: The Role of Diet and Oxidative Stress in a Gender-Specific Disorder. *Biomedicines* 2023;11:450.
31 Alviggi C, Andersen CY, Buehler K, *et al*. A new more detailed stratification of low responders to ovarian stimulation: from a poor ovarian response to a low prognosis concept. *Fertil Steril* 2016;105:1452–3.
32 Pounis G, Bonaccio M, Di Castelnuovo A, *et al*. Polyphenol intake is associated with low-grade inflammation, using a novel data analysis from the Moli-sani study. *Thromb Haemost* 2016;115:344–52.
33 Shi H, Schweren LJS, Ter Horst R, *et al*. Low-grade inflammation as mediator between diet and behavioral disinhibition: A UK Biobank study. *Brain Behav Immun* 2022;106:100–10.
34 Jones G, Kennedy S, Barnard A, *et al*. Development of an endometriosis quality-of-life instrument: The Endometriosis Health Profile-30. *Obstet Gynecol* 2001;98:258–64.
35 Breivik H, Borchgrevink PC, Allen SM, *et al*. Assessment of pain. *Br J Anaesth* 2008;101:17–24.
36 Rosen C, Brown J, Heiman S, *et al*. The Female Sexual Function Index (FSFI): A Multidimensional Self-Report Instrument for the Assessment of Female Sexual Function. *J Sex Marital Ther* 2000;26:191–208.
37 Galati G, Somigliana E, Ciaffaglione M, *et al*. Follicular steroidogenesis in random start protocols for oocyte cryopreservation. *J Assist Reprod Genet* 2023;40:2149–56.
38 Invernici D, Reschini M, Benaglia L, *et al*. The impact of endometriosis on IVF efficacy: qualitative and quantitative assessment of ovarian response and embryo development. *Reprod Biomed* 2022;45:275–81.
39 Chan A-W, Tetzlaff JM, Gøtzsche PC, *et al*. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
40 Hopewell S, Chan A-W, Collins GS, *et al*. CONSORT 2025 statement: updated guideline for reporting randomised trials. *BMJ* 2025;389:e081123.
41 Lin T, Allaire C, As-Sanie S, *et al*. World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonization Project: V. Physical examination standards in endometriosis research. *Fertil Steril* 2024;122:304–15.
42 Guerriero S, Condous G, van den Bosch T, *et al*. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. *Ultrasound Obstet Gynecol* 2016;48:318–32.
43 Decarli A, Franceschi S, Ferraroni M, *et al*. Validation of a food-frequency questionnaire to assess dietary intakes in cancer studies in Italy. Results for specific nutrients. *Ann Epidemiol* 1996;6:110–8.
44 Visser E, de Jong K, van Zutphen T, *et al*. Dietary Inflammatory Index and Clinical Outcome Measures in Adults With Moderate-to-Severe Asthma. *J Allergy Clin Immunol Pract* 2023;11:3680–9.
45 Shivappa N, Steck SE, Hurley TG, *et al*. A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal Variation of Blood Cholesterol Study (SEASONS). *Public Health Nutr* 2014;17:1825–33.

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

46 Kyle UG, Bosaeus I, Lorenzo AD, *et al*. Composition of the ESPEN Working Group. Bioelectrical impedance analysis--part I: review of principles and methods. *Clin Nutr* 2004;23:1226–43.
47 Kyle UG, Bosaeus I, De Lorenzo AD, *et al*. Bioelectrical impedance analysis-part II: utilization in clinical practice. *Clin Nutr* 2004;23:1430–53.
48 Hoffmann TC, Glasziou PP, Boutron I, *et al*. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:bmj.g1687.
49 Lorenz MW, Graf M, Henke C, *et al*. Anthropometric approximation of body weight in unresponsive stroke patients. *J Neurol Neurosurg Psychiatry* 2007;78:1331–6.
50 Peng X, Li X, He J, *et al*. Ultra-Processed Food Consumption and the Risk of Psoriasis: A Large Prospective Cohort Study. *Nutrients* 2025;17:1473.
51 Wilmes L, Caputi V, Bastiaanssen TFS, *et al*. Sex specific gut-microbiota signatures of resilient and comorbid gut-brain phenotypes induced by early life stress. *Neurobiol Stress* 2024;33:100686.
52 Zheng X, Zhang W, Wan X, *et al*. The effects of Mediterranean diet on cardiovascular risk factors, glycemic control and weight loss in patients with type 2 diabetes: a meta-analysis. *BMC Nutr* 2024;10:59.
53 Duffy JMN, Bhattacharya S, Bhattacharya S, *et al*. Standardizing definitions and reporting guidelines for the infertility core outcome set: an international consensus development study. *Fertil Steril* 2021;115:201–12.

BMJ Open: first published as 10.1136/bmjopen-2025-108596 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on January 15, 2026 by guest. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.