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REVIEW ARTICLE

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Consensus conference results on contraception in women beyond 40 years of age

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ABSTRACT

Objective: The objective is to develop expert consensus to inform clinical decision-making in the use of hormonal contraceptives in women over 40 years of age. **Methods:** A multidisciplinary panel organised by the Italian Society of Contraception performed a systematic literature review up to October 2024, defining the priorities in the choice of a contraceptive and its effects on cardiovascular risk, menstrual bleeding, bone health, and sexual function associated with hormonal contraception in women over 40. Statements summarising the findings were discussed and refined in a dedicated expert meeting. Final statements were presented and subjected to anonymous voting at a national congress, where consensus was defined as a minimum of 75% agreement. **Results:** Ninety-five to ninety-nine percent of participants endorsed seven consensus statements. Cardiovascular safety is recognised as the primary factor in the selection of contraceptives. The use of progestogen-only methods is considered safe for cardiovascular risk. Combined hormonal contraceptives utilising natural oestrogens or 20 mcg ethynylestradiol in conjunction with non-androgenic progestins are considered more advantageous for the cardiovascular risk profile. The levonorgestrel intrauterine device, oestradiol valerate/dienogest, and the combined contraceptive vaginal ring are identified as the most effective options for menstrual management. The type of hormone and its route of administration can influence sexual function, with implants and vaginal rings showing positive effects. Combined hormonal contraceptives demonstrate protective effects on bone density, whereas progestogen-only methods exhibit a neutral impact. **Conclusions:** This Italian consensus provides evidence-based guidance on hormonal contraceptive choices for women over 40, incorporating non-contraceptive effects to support individualised care during perimenopause.

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Introduction

Eligibility criteria for contraceptive use divide women below and above 35–40 years of age, the latter requiring a specific guideline, being at higher risk of metabolic and cardiovascular disease [1,2]. The perimenopausal period presents unique health considerations for women over 40. Despite declining fertility, the risk of unintended pregnancies remains a significant concern [3]. This life stage is defined by substantial physiological shifts, primarily driven by fluctuations in oestrogen and progesterone levels, leading to menstrual irregularities, heavy menstrual bleedings [3–6], increase of perimenopausal symptoms [7], decreased sexuality [8,9], metabolic alterations, increased body mass index (BMI) and visceral fat [10,11], and increased bone loss [12]. Hormonal contraception is frequently prescribed during this

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period, not only for pregnancy prevention but also for managing menstrual cycle irregularities and abnormal bleeding [3–6]. Additionally, potential non-contraceptive benefits are often considered, such as mitigation of bone loss [13,14] or potential improvement of sexual function [8]. Yet the effects of different hormonal contraceptive methods can vary significantly; some may offer benefits in certain areas while potentially having negative impacts on other aspects like the cardiovascular system [11].

Considering the variable benefits and risks associated with hormonal methods in perimenopausal women, along with the limited evidence regarding their non-contraceptive effects, we opted for a formal consensus process instead of a standalone review or guideline. This methodology facilitates the systematic aggregation of conflicting data and expert interpretation, resulting in clear, evidence-based recommendations.

The aim of this consensus exercise is to synthesise current evidence on the positive and negative non-contraceptive effects of hormonal contraception in women over 40.

Methods

This consensus statement, sponsored by the Italian Society of Contraception (SIC), was developed using a structured approach that combined a systematic literature review, expert panel assessment, and formal consensus-building in line with ACCORD guidelines [15]. Although the protocol was prospectively designed, it was not registered online. Figure 1(A) illustrates the development timeline. Two co-chairs led the process, developing the methodology, overseeing procedures, and facilitating discussions, and appointed a

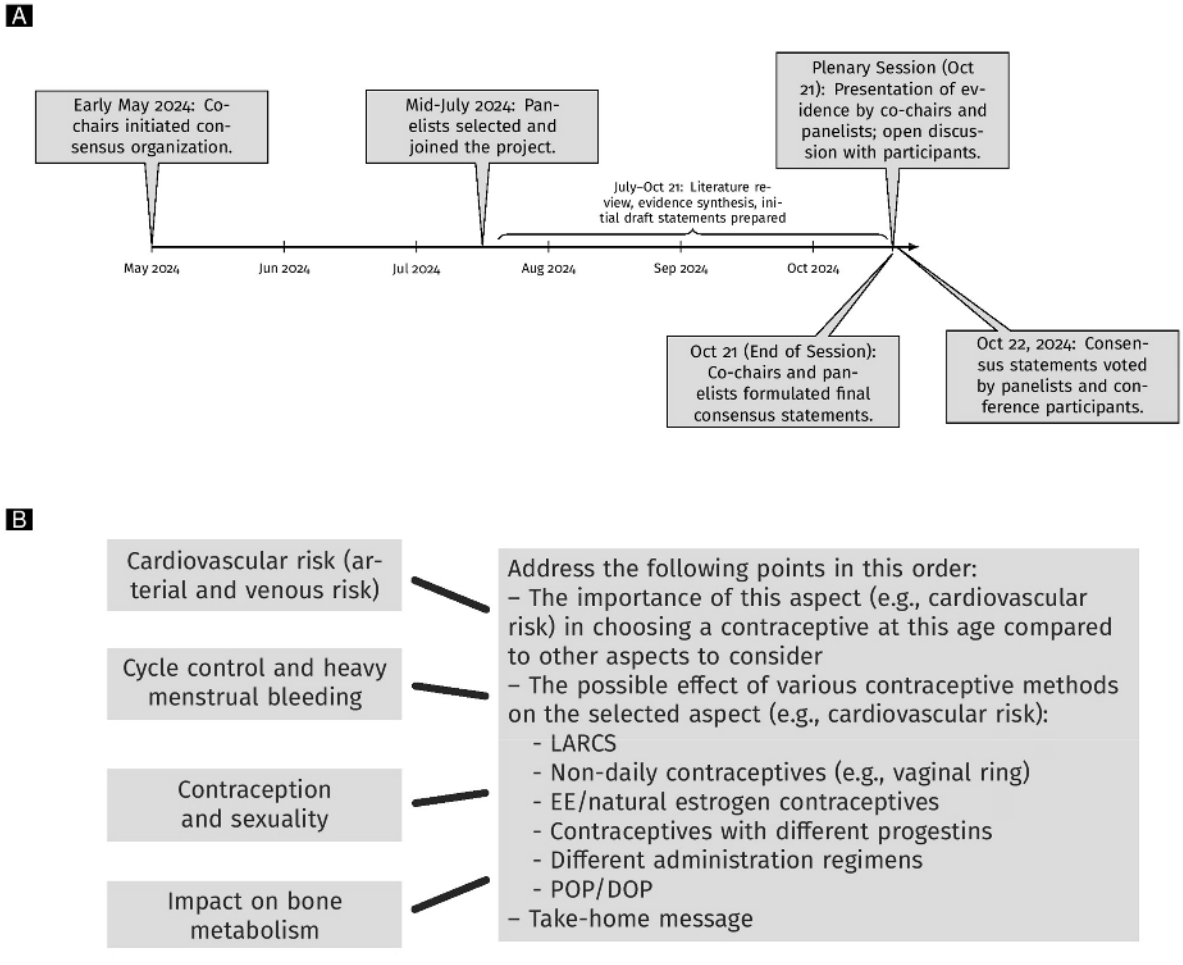


Figure 1. Panel A shows the schematic overview of the consensus timeline, outlining the sequence of activities, including organisation initiation, evidence preparation, plenary discussion, and statement finalisation and voting. Panel B shows the overview of the four assessed domains (cardiovascular risk, cycle control/HMB, sexuality, and bone metabolism) and the required discussion points concerning contraceptive choice and effects.

five-member expert panel. Each panellist was assigned a specific subject for evidence retrieval and summary preparation, as outlined in Figure 1(B). Details of the co-chairs and panellists are provided in Table 1.

Expert panel and literature review

Panel members in charge of the specific argument independently reviewed the current scientific literature on the non-contraceptive effects (both positive and negative) of hormonal contraception (including various progestins, oestrogens, and delivery routes), focusing specifically on women over the age of 40. A systematic literature search was conducted utilising PubMed (including Medline) and Scopus databases, spanning records from their inception through October 20, 2024. The search strategy targeted studies investigating the various impacts of hormonal contraception. Core terms defining the intervention (contraception, contraceptive, or "hormonal contraception") were combined with distinct terms relevant to specific domains of interest. The domain examining the impact on bone metabolism included search terms related to bone health, osteoporosis, or "bone mineral density." For cardiovascular risks, both venous and arterial, the search encompassed a broad range of terms, including "cardiovascular risk," "heart disease," "blood clots," thromboembolism, stroke, "myocardial infarction," "venous thrombosis," "arterial thrombosis," and embolism. To investigate sexuality, the search integrated terms associated with sexual health, such as sexuality, "sexual function," libido, or "sexual satisfaction." The domain addressing cycle control and heavy menstrual bleeding included specific terms like "heavy menstrual bleeding," menorrhagia, "menstrual flow," "cycle control," "irregular bleeding," or "menstrual regulation." Records deemed potentially relevant were subjected to an independent full-text review by panel members. Articles were included if they were peer-reviewed, provided scientifically robust data, and examined the non-contraceptive effects of hormonal methods in women over 40. In cases where age-specific evidence was lacking, studies reporting general non-contraceptive effects of these methods were also considered. The expert panel prioritised high-level evidence, systematic reviews, meta-analyses, and clinical guidelines over individual primary studies to balance comprehensiveness with practical constraints, with a particular emphasis on data relevant to the Italian context. To enhance coverage, we augmented database searches with backward citation tracking of significant papers and included additional references recommended by panellists. Only contraceptive methods approved in Italy were included; for instance, norethindrone acetate and medroxyprogesterone acetate, which are not available for contraception in the country, were excluded. Subsequently, relevant studies published between the consensus and manuscript preparation were incorporated into the references without altering the consensus content.

Statement development and refinement

Following the literature review, each expert proposed draft statements summarising key findings, potential benefits, risks, and clinical considerations. These initial statements formed the basis for discussion during a dedicated expert consensus meeting on the plenary section of October 22, 2024, at the national meeting of the Italian Society of Contraception (15th National Congress of the Italian Society of

Table 1. List of conference co-chairs and panelists, detailing their roles and specific areas of expertise presented.

Member	Role	Area of expertise
Angelo Cagnacci	Co-chair and Panellist	International expert in gynecological endocrinology, with specific expertise in contraception and menopause
Franca Fruzzetti	Co-chair	International expert in gynecological endocrinology, with specific expertise in hormonal contraception and endocrinology.
Alessandro Gambera	Panellist (presenter of cycle control and heavy menstrual bleeding)	Expert in gynecological endocrinology, with specific expertise in hormonal contraception.
Gloria Bonaccorsi	Panellist (presenter of impact on bone metabolism)	Expert in gynecological endocrinology, with specific expertise in menopause, hormonal contraception, and metabolic changes during female ageing.
Maurizio Guida	Panellist (presenter of contraception and sexuality)	Expert in contraception, including research on innovative hormonal administration methods (vaginal rings, implants) and family planning.
Vincenzina Bruni	Panellist (presenter of cardiovascular risk (arterial and venous risk))	International expert in Gynecological Endocrinology and Paediatric and Adolescent Gynaecology.

Contraception held in Stresa in 2024). In this meeting, all proposed statements were presented, critically evaluated, debated, and collectively revised by the panel members to ensure clarity, accuracy, and clinical relevance based on the synthesised evidence and expert opinion. After the plenary session, the final statements were prepared by the co-chairs and the expert panel members.

Consensus voting

The refined set of statements resulting from the expert meeting was subsequently presented during the plenary session held on October 23, 2024, of the same National meeting (Figure 1(A)). Consensus on the final statements was assessed by anonymous voting among the panellists and conference participants. The vote was performed by the electronic system. Using a personal device, each participant scanned a QR code that redirected to the voting page (using appropriate limiting methods, each device was allowed one vote for each statement). The attendees represented gynaecologists working in public and private hospitals, territorial facilities, or private practice representatives of the different Italian geographical areas. All registered participants attending the session were invited to vote on each statement. Voting was conducted using a binary response format, where participants could express "agree" or "disagree" with the presented statement. The level of agreement for each statement was recorded. A statement was considered to have achieved consensus if it received agreement from a predefined majority: 75% of the voting participants. Table 2 shows the terminology used in this consensus. Furthermore, all the proposed statements are presented in Table 3.

Results

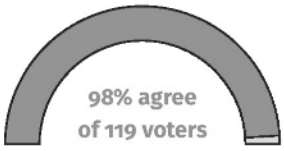
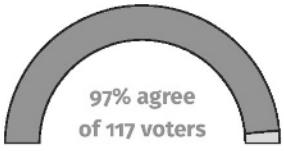
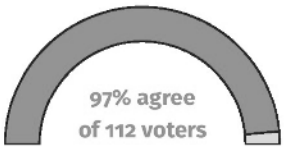
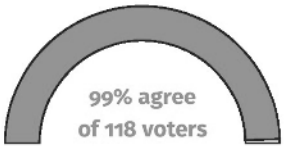
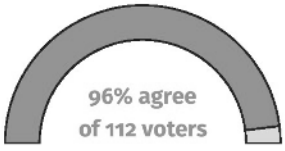
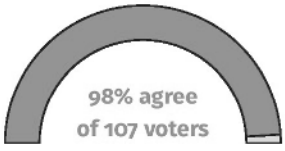
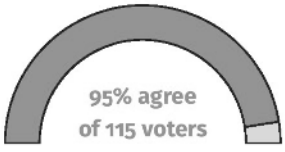
Timeline and participant engagement of the consensus process

The consensus timeline is presented in Figure 1(A). All the panellists actively contributed to the final consensus statements. During the presentation of the evidence, an average of 150 conference participants were present in the plenary section. During the plenary section for the consensus expression, an average of 114 conference participants expressed their opinions on the final statements.

Table 2. Terminology encompassing pertinent hormones and contraceptive methods along with their acronyms, as outlined in the consensus.

Hormones and contraceptive methods	Acronym
Hormones	
Oestrogens	
Ethinylestradiol	EE
Oestradiol	E2
Oestradiol valerate	E2V
Estetrol	E4
Progestins	
Levonorgestrol	LNG
Gestodene	GSD
Norgestimate	NGM
Desogestrel	DSG
Etonogestrel	ENG
Norelgestromin	NGMN
Drospirenone	DRSP
Dienogest	DNG
Contraceptive methods	
Combined hormonal contraceptives	CHCs
Combined oral contraceptives	COCs
Patch	
Combined contraceptive vaginal ring	CVR
Progesterone only contraceptives	POCs
Progestogene-only pill (DSG)	POP
Drospirenone-only pill (DRSP)	DOP
Implants (ENG)	
Levonorgestrel-releasing intrauterine system	LNG-IUS

Table 3. Consensus statements on hormonal contraception for women over 40, outlining factors influencing choice, specific considerations (cardiovascular risk, cycle control, heavy menstrual bleeding, sexuality, bone effects), and the percentage of agreement among voters for each statement (consensus defined as ≥75% agreement).

N	Statement	Votes
1	**Factors that can influence the choice of contraception after 40 years old**: • **Cardiovascular safety regarding arterial risk and venous risk** • In later stages, the choice is influenced also by: ○ Menstrual irregularity and menorrhagia (heavy bleeding) ○ Changes in sexuality ○ Loss of bone mass	
2	**Venous Risk**: • Any form of **oestrogen-free contraception**, both long-acting (implant, LNG-IUS) and short-acting (POP, DOP), does not increase the risk of VTE. • Combinations with **EE/LNG, EE/NGM**, and those with **natural oestrogens** (oestradiol) are the ones that least increase the risk of VTE compared to other combinations with EE. • **Regarding the ring and the patch**, there is conflicting data on whether or not they increase the risk of VTE compared to the reference EE/LNG.	
3	**Arterial Risk**: **Progestogen-only** contraception, both long-acting and short-acting, does not increase arterial risk. Combinations of **EE (ethinylestradiol) and androgenic progestogens**, especially LNG (levonorgestrel), increase the risk of myocardial infarction (heart attack) and also ischaemic stroke. The combination with a **low level of EE (20 mcg) with non-androgenic progestogens** (DRSP) does not increase the risk. Combinations with **natural oestrogens** (oestradiol), in post-marketing studies, do not increase arterial risk.	
4	**Cycle control**: • In case of **menstrual irregularity**, the combinations **vaginal ring (EE/ENG) and EE/NGM** are those that best ensure menstrual regularity and most reduce unexpected bleeding. • Combinations with **higher EE dosages (>30mcg)** control the cycle better than those with lower levels of EE and natural oestrogens.	
5	**Heavy menstrual bleeding**: • In case of heavy menstrual bleeding, the most effective approaches are, in **descending order**: ○ LNG-IUS 52 mg ○ E2V/DNG ○ Ring (EE/ENG) ○ COC (EE 35 mcg or 30 mcg) ○ POP or DOP	
6	**Sexuality**: • Sexuality is influenced by biological, psychological, relational, and socio-cultural factors. • The contraceptive approach **improves sexuality by ensuring the reduction of the risk of unwanted pregnancies**. • Better to use **natural oestrogens** for low impact on SHBG or low-dose EE (20 mcg) with an androgenic progestin. • **Vaginal ring**: possible positive effects (especially due to local effects). • **Implant**: limited uncontrolled studies suggesting a positive effect. • **Androgenic POP**: undetermined effect. • **Anti-androgenic DOP**: undetermined effect. • **LNG-IUS**: neutral effects.	
7	**Effect on Bone** • Contraceptives in perimenopause: ○ **COC** protect against bone loss. ○ **POP, DOP** and **implants**: neutral effect (do not protect against bone loss). ○ **LNG-IUS**: neutral effect (does not protect against loss), although one retrospective epidemiological study shows a protective effect on fractures.	

The outcome of the consensus process

Factors that can influence the choice of contraception after 40 years old (panellist Angelo Cagnacci)

The determinants influencing the selection of contraceptive methods among women over 40 years of age have been established, with a primary focus on the cardiovascular safety of hormonal contraceptives. This focus on safety includes considerations of both venous thromboembolism (VTE) and arterial thromboembolism (ATE) [1,2]. During the perimenopausal transition, which generally occurs in the late forties,

various factors increasingly affect contraceptive choices among women. Menstrual irregularities, such as heavy menstrual bleeding (HMB), frequently occur due to hormonal fluctuations and anovulatory cycles typical of this stage [3–6]. Alterations in sexuality are associated with heightened occurrences of symptoms such as vaginal dryness and dyspareunia [8,9]. Bone loss significantly accelerates during the perimenopausal period [12,16]. Ninety-eight percent of voters concurred with the final statement presented in Table 3 (Statement 1). During this stage of life, the primary determinant affecting contraceptive selection is its safety concerning venous and arterial cardiovascular health. In later life, the decision is influenced by the potential positive impact on menstrual irregularity, heavy menstrual bleeding (HMB), sexual health, and bone density.

Cardiovascular safety (panellist Vincenzina Bruni)

Venous risk

According to current evidence, progestin-only pills (POPs) do not elevate the VTE risk [17–19]. Two Danish national registry studies found no significant difference in VTE risk between control groups and users of POP, drospirenone-only pill (DOP), or implants and identified a protective effect associated with levonorgestrel intrauterine system (LNG-IUS) use [20–22]. Additionally, one study examining women with personal or familial histories of VTE or hereditary thrombophilia found no association between POP use and VTE risk [18]. Current data suggest that combined oral contraceptives (COCs) containing LNG or norgestimate (NGM) exhibit the lowest risk of VTE among ethynyl-oestradiol (EE)-based combinations [23]. A network meta-analysis indicated that COCs containing LNG with either 20 mcg or 30 mcg EE were among the safest options regarding VTE risk [24]. Two Danish national registry studies confirmed the lower VTE risk associated with LNG than desogestrel (DSG), gestodene (GSD), or drospirenone (DRSP) combination with EE [20–22]. Postmarketing surveillance study indicated that oestradiol valerate (E2V) and dienogest (DNG) had similar VTE incidence rates than COCs containing LNG, actually lower when only data of idiopathic thrombosis were considered [25,26]. A VTE risk similar to EE/LNG was also reported for oestradiol (E2) associated with nomegestrol acetate (NOMAC) in another postmarketing study [27], and a similar VTE incidence rate between COCs containing E2 and COCs with EE with LNG was recently reported in a Danish national registry study [22]. The available data on the VTE risk profile of E4 are inadequate for forming definitive conclusions. There is insufficient evidence to determine whether the contraceptive patch or CVR carries a different VTE risk compared to COCs [23,28]. Studies from Finnish and Danish national registry studies reported that the contraceptive patch (EE/norelgestromin) and the vaginal ring (EE/etonorgestrel) were associated with a VTE risk higher than that of oral EE/LNG preparations [19–22].

The final statement is reported in Table 3 (Statement 2), and 97% of the voters agreed that any form of oestrogen-free contraception, whether long-acting such as the implant or the LNG-IUS, or short-acting like POP or DOP, does not increase the risk of VTE.

Arterial risk

Observational studies suggest that POPs are not associated with an increased risk of stroke or myocardial infarction [29,30]. Similar conclusions were reached in published metanalyses [29,31]. However, data on injectable or implantable progestins remain limited, with some studies suggesting a possible increased risk for ischaemic stroke with implants and DSG oral pills, though event numbers were low [30,31]. No progestin-only contraceptive is associated with an increased risk of myocardial infarction [30]. The use of LNG-IUS is not associated with an increased risk of either thrombotic stroke or myocardial infarction [30,32]. Evidence consistently shows that COCs containing EE may increase the risk of ATE [30,32,33]. This risk appears dose-dependent [32,33]. Combinations with EE 30-40 mcg and the second-generation, androgenic progestogen LNG are associated with increased ATE risk [30,32]. COCs containing EE 20 mcg with newer, less androgenic, or antiandrogenic progestogens like DRSP appear to have a more favourable profile. A Danish cohort study found that the risk for thrombotic stroke was slightly elevated for EE 20 mcg combined with DSG or GSD, and that of myocardial infarction only for EE 20 mcg and DSG [32]. Crucially, the relative risk for thrombotic stroke and myocardial infarction was not increased by EE 20 mcg combined with DRSP [32]. These data were confirmed by a larger Danish national study with data up to 2021 [30]. COCs containing natural oestrogens like E2, E2V, or estetrol (E4) were developed to improve

the cardiovascular safety [25,34]. Postmarketing surveillance and observational studies provide preliminary evidence supporting this. The INAS-SCORE study, comparing E2V/DNG to other COCs, including EE/LNG, found lower incidence rates of ATE among E2V/DNG users than among users of other COCs or EE/LNG [25]. Yet the number of events was very low, precluding robust statistical comparison [25]. There is no clear epidemiological study with COCs containing estetrol, although its cardiovascular safety is suggested by available clinical studies [34,35].

The final statement is reported in Table 3 (Statement 3), and 97% of the voters agreed that progestogen-only contraception, whether long-acting or short-acting, does not elevate the risk of ATE; instead, this risk is heightened by combinations of EE 30-40 mcg and LNG. Combinations containing EE 20 mcg and DRSP do not increase ATE risk, and combinations with natural oestrogens appear unlikely to increase this risk.

Cycle control and heavy menstrual bleeding (panellist Alessandro Gambera)

Cycle control

The vaginal ring, which delivers EE and etonogestrel (ENG), has shown effective cycle regulation. Research indicates a low incidence of irregular bleeding (spotting or breakthrough bleeding during usage), often demonstrating superior performance compared to some COCs with higher doses of EE [36,37]. The combination of 30–40 mcg EE and NGM in oral formulations demonstrates effective cycle control [38,39]. COC combinations containing EE 30–40 mcg promote endometrial stability, resulting in more predictable menstrual cycles and a reduced incidence of unscheduled breakthrough bleeding or spotting compared to those with EE 20 mcg [36,37,39]. Historically, substituting EE with less potent natural oestrogens, such as oestradiol (E2) or its prodrug oestradiol valerate (E2V), has posed challenges in achieving satisfactory cycle control, frequently leading to increased rates of bleeding irregularities [36,37,39].

The final statement is reported in Table 3 (Statement 4), and 99% of the voters agreed that regarding cycle control, in case of menstrual irregularity, the combinations vaginal ring (EE/ENG) and EE/NGM are those that best ensure menstrual regularity and most reduce unexpected bleeding. Combinations with higher EE dosages (>30mcg) control the cycle better than those with lower levels of EE and natural oestrogens.

Heavy menstrual bleeding

The statement ranking is supported by evidence synthesised mainly in systematic reviews and network meta-analyses [40–44]. The evidence suggests that LNG-IUS (containing 52 mg LNG) is often a highly effective first-line medical treatment for HMB [40–44]. The use of LNG-IUS (52 mg) results in a considerable reduction in bleeding, significantly more than other medical therapies [40,42]. It is associated with improved quality of life compared to other medical treatments and comparable satisfaction rates to surgical options like endometrial ablation or hysterectomy in the longer term [40,42,45,46]. Network meta-analyses indicate that menstrual blood loss is reduced more by LNG-IUS than COCs [42]. Among COCs, those containing E2V and dienogest (DNG) are effective and licenced for the treatment of HMB [47–50]. The vaginal ring containing EE and ENG was found effective in reducing menstrual blood loss and showed a better performance than COC with higher levels of EE [41,51–53]. COCs, including those with 30–40 mcg of EE, are more effective for HMB than those containing lower EE levels [37,39,54]. These formulations often contain progestins like NGM or LNG [41,42,55–57]. In a recent network meta-analysis COCs are ranked below the vaginal ring for HMB [42]. Although there is limited data for POP or DOP, as for LNG-IUS, they can be used in women with an increased cardiovascular risk. The DOP, specifically a 4 mg DRSP dose in a 24/4 regimen, has been developed to improve the often problematic bleeding profiles associated with traditional POPs. Studies show it provides a better bleeding profile (less unscheduled bleeding) compared to DSG POP [58], but its efficacy on HMB is unproven [59].

The final statement is reported in Table 3 (Statement 5), and 96% of the voters agreed that in the case of HMB, the most effective approaches are, in descending order: LNG-IUS 52 mg, E2V/DNG,) vaginal ring, 30–40 mcg EE COC and POP/DOP.

Sexuality (panellist Maurizio Guida)

Sexuality is a complex and multifactorial aspect of life, influenced by biological, psychological, relational, and socio-cultural factors [60,61]. A complete understanding of women's sexual function requires the individual assessment of these factors and a biopsychosocial approach recognising the interplay between these elements [60]. The use of contraception can positively affect sexuality by alleviating the fear of unplanned pregnancies, which is always possible even at the end of the female fertile phase [61–65]. By separating sexual activity from procreation, contraception may allow for a greater focus on pleasure and intimacy, potentially improving overall sexual well-being [62,64,65]. For hormonal contraception, the type and dosage of hormones can influence sexual function. It is suggested to prefer hormonal contraceptives with a minimal impact on sex-hormone binding globulin (SHBG) to avoid hypoandrogenism, like COCs with natural oestrogens [14,61,66]. Different studies also indicate that women with COC-associated female sexual dysfunction can improve several sexual domains after switching to a combined E2V/DNG pill or a COC containing E2/NOMAC [67,68]. Some evidence suggests that using EE 20 mcg combined with an androgenic progestogen might be preferable [61,69]. The vaginal ring has shown possible positive effects on sexuality, potentially due to the local impacts [62,70]. A controlled study comparing oral EE 20 mcg/DSG and the vaginal ring reported similar improvements in the assessed sexuality parameters, with the vaginal ring uniquely associated with an increase in sexual fantasy [62]. Furthermore, the vaginal ring might increase lubrication and a healthy vaginal microbiota [61]. Another study reported more sexual desire with the vaginal ring than EE 20 mcg/DSG [71]. A single prospective, non-comparative study of the etonogestrel subdermal implant indicated in an Italian population enhancements in sexual function, including pleasure, personal initiative, orgasm, and satisfaction, alongside decreases in anxiety and discomfort [64]. Information on androgenic POP and DOP is limited. A randomised controlled trial on an LNG-based POP, which is not available in Italy, reported a neutral effect on sexuality [72]. Some authors have suggested that the effects of POCs may vary according to their androgenic or anti-androgenic properties; however, specific data regarding the formulations available in Italy are lacking [73]. A comparative study found POP's effect on desire was less effective than the vaginal ring, though further research is needed to clarify progestin-specific impacts [71]. COCs with antiandrogenic progestins do not seem to negatively impact sexuality. In a prospective study, EE 30 mcg/DRSP increased sexual enjoyment and satisfaction, orgasm frequency, arousal, and frequency of sexual activity [74]. More recent studies indicate that COCs with DRSP and DNG positively influence sexuality [60,74–77]. The LNG-IUS generally shows neutral effects on sexuality. Studies comparing LNG-IUS users to copper-intrauterine device (Cu-IUD) users found no significant differences in sexual function overall or within psychological domains [61]. This finding suggests that the LNG-IUS does not typically negatively impact sexual function and can be a valid option for women experiencing distressing sexual problems with other hormonal contraceptives [61].

The final statement is reported in Table 3 (Statement 6), and 98% of the voters agreed that sexuality is influenced by biological, psychological, relational, and socio-cultural factors. Furthermore, it was noted that the contraceptive approach improves sexuality by ensuring the reduction of the risk of unplanned pregnancies. Regarding hormonal impact, it is considered better to use natural oestrogens for a low impact on SHBG or low-dose EE (20 mcg) combined with an androgenic progestogen. Different contraceptive methods show varying effects: the vaginal ring may have positive effects, particularly due to local action, and implants also demonstrate positive effects. POPs generally yield positive effects on sexuality, whereas DOP tends to have a negative impact. Finally, the LNG-IUS is considered neutral on sexuality. It is also crucial to acknowledge the individuality of each woman's sexual response across various methods. While a particular contraceptive may improve sexual well-being for some, it may have a different or even negative effect on others. Therefore, the selection of a method should be tailored to the individual.

Bone metabolism (panellist Gloria Bonaccorsi)

Women naturally experience bone loss during perimenopause [78], and combined hormonal contraceptives can potentially protect against this bone loss [16,78–81]. Research on the effects of

contraceptives on bone health predominantly examines bone metabolism markers and bone mineral density (BMD), with limited data on fracture risk. The impact of contraceptives on bone health is influenced by factors such as age, individual risk factors, oestrogen dosage and type, and progestin selection [14,82]. Data in oestrogen-deficient women indicate that sustaining circulating oestradiol levels above 30 pg/mL may reduce bone loss during the perimenopausal transition, ideally using natural oestrogens (e.g. E2V) or combinations with an androgenic progestin [83–85]. In a longitudinal evaluation, various low-dose COC formulations were protective, helping maintain bone mineral density in perimenopausal women [16]. POP, DOP, and contraceptive implants appear to exert a neutral impact on bone health in perimenopausal women. Oestradiol levels during POP, DOP, and implant use correspond to the early follicular phase, implying that no accelerated bone loss occurs during their use [86]. There is no published study directly assessing the impact of POP use on BMD, and no study reported adverse effects on BMD with implants (ENG) [87]. There are currently no published data on their association with bone fractures [87–90]. Relying on the production of endogenous oestradiol by the ovary POP, DOP and Implant are not protective on bone when the ovary reduces its activity. The LNG-IUS is generally considered neutral regarding bone health [78,91]. Most available evidence supports a neutral impact on bone mineral density [91–96]. Notably, a retrospective study revealed no significant difference in BMD changes between Cu-IUD and LNG-IUS users, but a protective effect against bone fractures was observed [97].

The final statement is reported in Table 3 (Statement 7), and 95% of the voters agreed that, concerning the effect on bone during perimenopause, combined hormonal contraceptives protect against bone loss, while POP, DOP, and implants have a neutral effect and do not protect against bone loss. Similarly, the LNG-IUS generally has a neutral effect, although one retrospective study suggested a reduction of fractures.

Discussion

This consensus synthesised current evidence on the non-contraceptive impacts of hormonal contraception in women over 40 years and provided practical guidance tailored to the Italian context. The process combined a systematic literature review with expert panel deliberations and anonymous electronic voting to achieve robust recommendations.

Strengths and limitations

The methodological rigour of this consensus process, adhering to ACCORD guidelines and integrating systematic literature review with expert panel evaluation, represents a key strength, ensuring recommendations are evidence-based. The multifaceted nature of the panel provided a comprehensive perspective on key issues like cardiovascular risk, bone health, cycle control, and sexual function. High participant engagement (average 150 attendees, 114 voters) and broad final agreement further bolster the validity of the consensus outcomes. Moreover, anonymous electronic voting for the final statements enhanced objectivity by minimising individual bias among the large audience. Nonetheless, there are inherent limitations. The panel's composition and focus predominantly reflect the Italian context, which may restrict global generalisability despite similarities with the European landscape. The literature review revealed considerable variability in study designs, patient demographics, settings, and outcome measures, potentially impacting the consistency and applicability of the recommendations. The final vote was anonymous; however, the interactive nature of the prior open discussions may have influenced participant opinions. The potential for non-anonymized feedback to influence opinions prior to the final anonymous assessment signifies a limitation intrinsic to interactive consensus-building formats. In areas with limited high-quality empirical evidence, we depended on expert opinion based on clinical experience; while essential, these assessments inherently possess a degree of subjectivity. Finally, although our methodology was designed prospectively, we did not conduct formal prospective protocol registration. The lack of a pre-registered framework constitutes an additional limitation of this study.

Consistency with pre-existing literature

Although no similar consensus previously focused on the non-contraceptive effects of hormonal contraception in women over 40, the Faculty of Sexual and Reproductive Healthcare (FSRH) published a guideline on contraception for this age group [1]. While the FSRH guideline primarily discusses contraceptive effectiveness (this topic was outside our consensus scope), there are notable similarities and differences between the two documents. Both guidelines emphasise cardiovascular safety as a primary concern for contraception choice in women over 40 [1] and agree that combined hormonal contraceptives may protect against bone loss, whereas progestin-only contraceptives generally have neutral bone effects. The French College of Gynaecologists and Obstetricians (CNGOF - Collège National des Gynécologues et Obstétriciens Français) has also published a guideline for contraception for individuals over 40 years of age [98]. The CNGOF guideline states that chronological age alone does not contraindicate any contraceptive method, emphasises cardiovascular safety, and recognises the non-contraceptive benefits of combined hormonal contraception, such as cycle regularisation and bone preservation, while emphasising the need for annual reassessment of risk factors [98]. Differences appear in specificity and detail regarding cycle control; our consensus explicitly favours the vaginal ring and COCs containing EE/NGM, highlighting better control with EE doses above 30 mcg. In contrast, the FSRH guideline does not rank methods explicitly but acknowledges poorer cycle control with lower EE doses [1]. The CNGOF guideline did not distinguish among various CHCs [98]. For HMB, our consensus offers a detailed efficacy ranking among hormonal contraceptives, aligning closely with a recent Cochrane meta-analysis, albeit the latter includes non-contraceptive methods [42]. Both our consensus and the FSRH guideline strongly support the LNG-IUS, though the FSRH guideline lacks detailed comparative rankings of other methods [1]. Additionally, other guidelines support the use of LNG-IUS as a first-line therapy for HMB, though they do not provide comparative rankings [1,98–100]. Our consensus also addresses in greater depth the nuanced impacts of hormonal contraception on sexuality, considering natural oestrogens, progestin types, and delivery methods. The FSRH guideline discusses libido and urogenital symptoms but less specifically links contraception to sexual outcomes [1]. The CNGOF guideline also emphasises the importance of addressing sexual comfort, yet it does not provide method-specific guidance [98]. Finally, our consensus highlights the potential cardiovascular safety of natural oestrogens and low-dose EE (20 mcg) combined with non-androgenic progestogens. In contrast, the FSRH guideline acknowledges that lower EE doses might mitigate risk but does not discuss natural oestrogens, and the progestin component of combined hormonal contraceptives [1]. The CNGOF guidelines also do not address the role of natural oestrogens [98]. While not exclusively aimed at women over 40, various international guidelines provide insights into contraceptive eligibility for this demographic. These include the World Health Organisation's Medical Eligibility Criteria (MEC) for Contraceptive Use [2], the UK Faculty of Sexual and Reproductive Healthcare MEC [101], and the U.S. Centres for Disease Control and Prevention's MEC [99]. All three prioritise cardiovascular safety as the primary concern; however, none distinguish risk based on the specific type of oestrogen or progestin in combined hormonal contraception (CHC). In alignment with existing guidelines and literature, we endorse progestin-only methods and intrauterine contraception as safer first-line options for women over 40 [1,2,98,99,101,102].

Conclusions

Selecting hormonal contraception for women over 40 requires balancing contraceptive needs with managing perimenopausal symptoms and considering non-contraceptive effects. This consensus, developed for the Italian context, synthesises current evidence and expert agreement on the impacts of various hormonal methods on cardiovascular risk, menstrual bleeding, sexual function, and bone health. The resulting recommendations provide a practical tool to support clinicians and women in making informed, personalised contraceptive choices during the perimenopausal transition in Italy.

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Authors contributions

CRediT: **Angelo Cagnacci**: Conceptualization, Data curation, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing; **Franca Fruzzetti**: Conceptualization, Data curation, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing; **Vincenzina Bruni**: Data curation, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing; **Alessandro Gambera**: Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing; **Maurizio Guida**: Data curation, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing; **Gloria Bonaccorsi**: Data curation, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing; **Ambrogio Pietro Londero**: Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing.

Ethical approval

The present study is exempt from ethical approval since this meta-analysis only involves anonymous data that has already been published.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

All data were extracted from previously published studies; thus, they are publicly available or presented in full in this article.

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