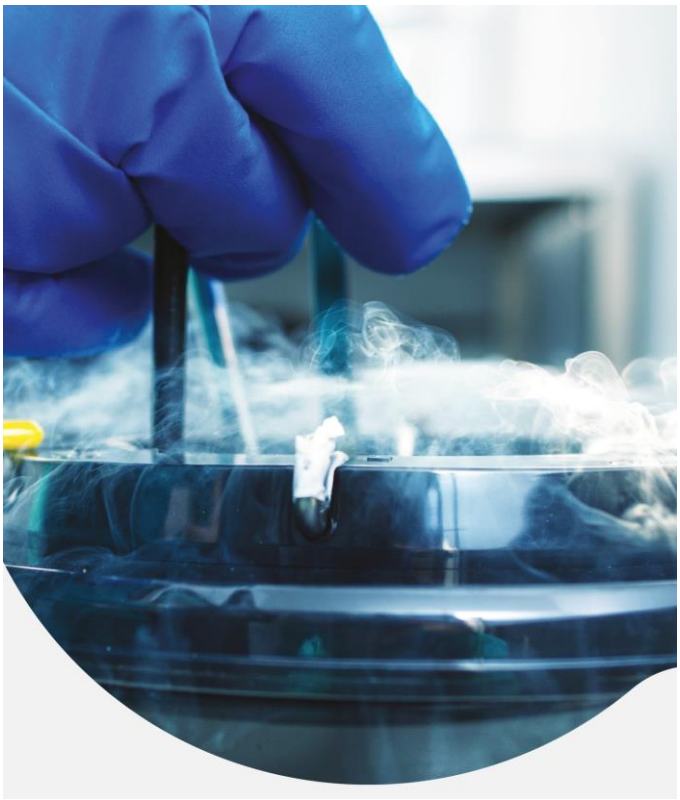

2020

ESHRE Female Fertility Preservation Guideline Development Group

Female Fertility Preservation

Guideline of the European Society of Human Reproduction and Embryology

REVIEW REPORT

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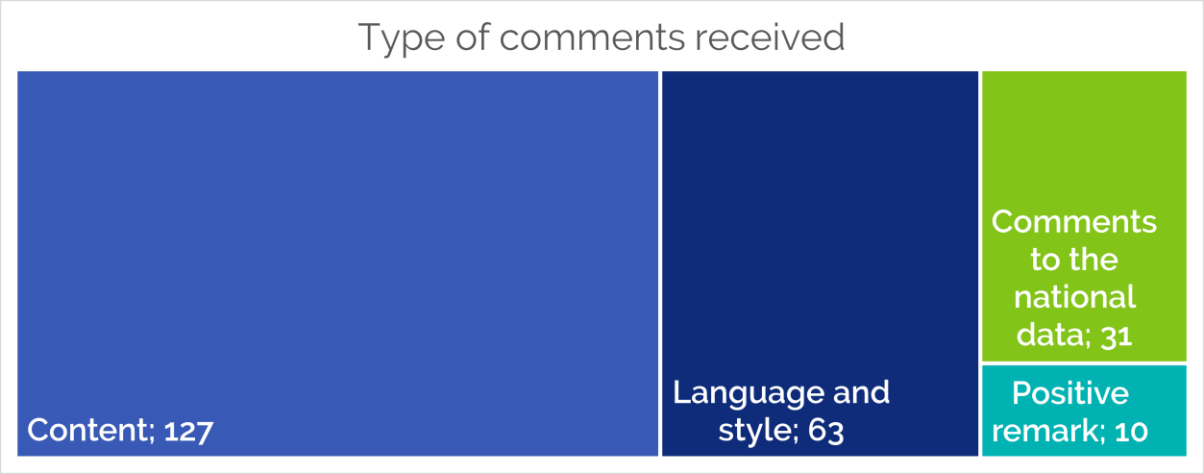
The draft of the guideline on Female Fertility Preservation was published for review for 6 weeks, between 6 May and 17 June 2020.

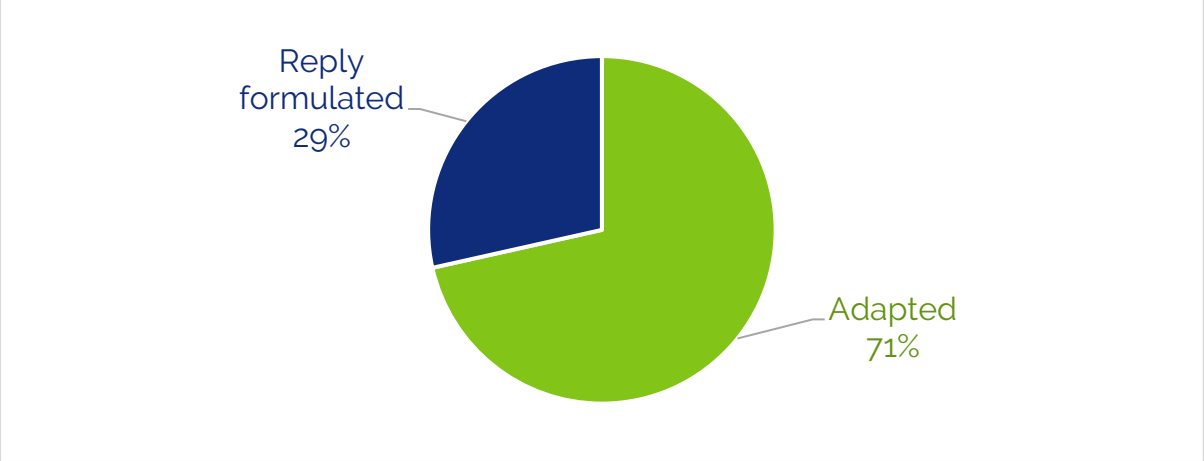
This report summarizes all reviewers, their comments and the reply of the guideline development group and is published on the ESHRE website as supporting documentation to the guideline.

During the stakeholder review, a total of 231 comments were received from 33 reviewers, including 9 representatives of professional organisations and 24 Individual experts.

The comments included 127 comments on the content of the guideline, 63 language and style corrections, 31 comments on the national data represented in tables 1 to 5, and 10 positive remarks that did not require a reply.



All comments were checked by the guideline development group and either addressed (in the guideline) or a reply was formulated. Most of the corrections for language and style (90.4%) and for the national data (90.3%) were adapted in the guideline. Of the 127 comments to the content of the guideline and the recommendations, 73 (57.4%) resulted in an adaptation to the text. Combined, 71.5% of the comments resulted in an adaptation or correction in the guideline text.



Experts that participated in the stakeholder review

The list of representatives of professional organization, and of individual experts that provided comments to the guideline are summarized below.

Representatives of professional organisations

Organisation	Country	Representative
Biologistes des Laboratoires d'Etude de la Fécondation et de la Conservation de l'oeuf (BLEFCO)	France	F.Brugnon, N.Achour Frydman, I. Aknin, N.Sermondade
British fertility Society – Policy and practice subcommittee and fertility preservation special interest group	UK	Ephia Yasmin and Melanie Davies
Groupement des gynécologues-obstétriciens de langue française de Belgique (GGOLFB)	Belgium	Henry Laurie
Hellenic Federation of cancer, ELL.O.K.	Greece	Margarita Chrysanthou Piterou
		Eleftheria Kourenta
International Federatin of Fertility Societies (IFFS)	USA	Linda Giudice
Oncofertility Consortium	USA	Teresa K. Woodruff
Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe gynécologie suisse (SGGG),	Switzerland	Sabine Steimann
The Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	Finland	Jarna Moilanen, Varpu Jokimaa, Noora Kaartinen, Maarit Niinimäki, Paula Kuivasaari-Pirinen, Hanna Hautamäki. Kaisu Luiro-Helve, Oskari Heikinheimo,

Individual experts

Reviewer	Country
Aboubakr Mohamed Elnashar	Egypt
Alexandra Kohl Schwartz	Switzerland
Bettina Böttcher, Bettina Toth	Austria
Carlos Calhaz-Jorge	Portugal
Dmitry Nikiforov	Denmark
E.E.L.O.Lashley	The Netherlands
Fernando J. Prados-Mondéjar	Spain
Gareth Greggains	Norway
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	Finland
Heidi Mertes	Belgium
Ira Winter	UK
Johan E J Smitz	Belgium
John Tzafetas	Greece
Kyle Orwig	USA
M.H.Mochtar	The Netherlands
Mahmoud Salama	USA
Michel De Vos - Ingrid Segers	Belgium
Miguel Moreno	Spain
Monica M Laronda	USA
Shelley Grant	USA/UK
Stefan Matik	North Macedonia
Stephan Gordts	Belgium
Teresa Almeida Santos	Portugal
Verena Nordhoff	Germany

Reviewer comments and replies

Name	Page	Line	Comment	Reply
Introduction, scope and general comments				
Kyle Orwig	1		Is female fertility preservation appropriate for transgender men? Perhaps should be fertility preservation for individuals with ovaries.	The guideline group attempted to be inclusive by including the 4 different populations, and transgender men. The documents title was also formulated to be inclusive. Changing it to "'individuals with ovaries" would probably not be appropriate for the 3 other patient groups.
Dr. Bettina Böttcher/ Prof. Dr. Bettina Toth	1		Thank you for all the effort and work! First remark: The title of the document changes to "recurrent pregnancy loss" when you start to save the document.	Thank you for this comment, this was corrected,
Shelley Grant	1	Para. 3	Replace "specific" with, "initially targeted or hoped for outcome" - Replace "nor does it establish … " with, "nor does it aim to set forth new standards of care	Our guidelines have a standard cover and standard disclaimer. We decided not to adapt this.
Shelley Grant	1	Para. 4	Replace "that are member of ESHRE" with, "and experts in fertility health research and education maintaining an active membership in ESHRE and its working groups."	Our guidelines have a standard cover and standard disclaimer. We decided not to adapt this.
Shelley Grant	1	Para. 5	Divide the sentence ending ", and is subject to change". Begin a new, second, sentence with, ". In response to new knowledge and changing social contexts, ESHRE reserves the right to periodically update recommendations and amend supporting documents as required."	Our guidelines have a standard cover and standard disclaimer. We decided not to adapt this.
Shelley Grant	5	11 to 12	Replace "'…, and make decisions" with, "have accepted the responsibility of providing patients the level and range of scientifically accurate information required for making informed decisions. It especially addresses the complexities involved in supporting decisions among patients scheduled to undergo gonadotoxic treatments or other procedures known to compromise fertility capacity. "	We have adapted the sentence to accommodate this comment
Shelley Grant	5	23	Replace "'… the widespread (though uneven)" with, "a significant increase interest for fertility preservation across new categories of female patients at all ages. While an analog to the established option of sperm cryopreservation used to	We have adapted the sentence to accommodate this comment

			retain the fertility capacity of post pubertal men, the range of patient and social concerns on female fertility have been shown to differ substantively."	
Shelley Grant	6	51	Add plans to address in detail (within a follow-up Guideline or publication) the unique concerns on broadening access to FP for adolescent and young adult patients, a motivated by medical and social reasons.	We currently do not have plans for a follow-up guideline or publications, so we decided not to add this information
Margarita Chrysanthou Piterou	6	42	As a general comment, I would prefer a FP guideline document focuses exclusively in cancer patients and their high risk family members.	The scope of the current guideline was determined by the ESHRE executive committee at the outset. Other guidelines specifically address cancer patients (e.g. ESMO guideline, shortly to be published).
Margarita Chrysanthou Piterou	6	48	There is another group of **healthy women** who carry a deleterious mutation in BRCA1/2. Almost a 50% of these women may receive chemotherapy, after an early onset breast cancer. They could form a separate group for FP counselling.	The relevance of BRCA mutations is included whenever specific information/recommendations could be made, for instance in section C2. Gonadotoxic treatments.
Mahmoud Salama	6	55	I really find no strong scientific reason to replace the term "Oncofertility". In fact, "Oncofertility" is now an established interdisciplinary field at the intersection of oncology and reproductive medicine in many countries around the globe that aims to provide effective fertility options to young cancer patients through several fertility preservation and restoration strategies. The term "oncofertility" was coined in 2006 by the Oncofertility Consortium, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA [1-4]. The Oncofertility Consortium produced many significant publications in the field over the past 14 years and some of them are already cited and discussed well in your great guideline draft. Best regards, Mahmoud	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table.
BFS	6	52	Terminology: In general, simpler terms are best ('egg freezing' rather than 'oocyte cryopreservation'). We should be writing for women as well as health professionals	Thank you for this comment. With regards to terminology, we followed previously published terminology (ICMART) and previous ESHRE papers. For a patient version, we will adapt terminology to ensure it is appropriate for patients.
Kyle Orwig	6	55	The term "Oncofertility" has become commonplace and can be used interchangeably with "fertility preservation in cancer patients". There is no need to strike the term from the ESHRE document.	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table,

Johan E J SMITZ	6	55	I don't see the utility of banning the term 'ONCOFERTILITY' , and change it for a series of 4 words … The term is now used for more than 10 years in all continents. and has It has been adopted in many WEBSITES by almost all organisations in the field of infertility and oncology . To my opinion this is NOT a useful recommendation.	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table,
Teresa Almeida Santos	6		There is no scientific reason to eliminate the term 'oncofertility' and replace it with 'FP in cancer patients'. For the purpose of continuity of the literature, there is no reason to place the term outside of the acceptable terminology grouping. Oncofertility is an established field of medicine and by eliminating it from acceptable terminology, you will lose a substantial amount of literature and awareness among providers and patients in Europe	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table,
Monica M Laronda	6	55	I am against replacing "oncofertility" with "FP in cancer patients". The term is easily recognizable and is defined in the Merriam-Webster dictionary. It is in frequent use, including in the text of this document (pages, 40, 43 and 96 and several citations). Dr. Teresa Woodruff, was elected into the National Academy of Inventors for coining this term and establishing the Oncofertility Consortium. The reason for making this terminology suggestion is not clear in the guidelines. Specifically stating that ESHRE guidelines recommend the use of "FP in cancer patients" over oncofertility could needlessly alienate a group of clinical and basic researchers who are valuable contributors to this field. I disagree that "oocyte cryopreservation" should be used instead of "egg freezing" or perhaps egg cryopreservation. Clinics are indeed freezing mature MII eggs. In this case, eggs is the appropriate term and should be used by experts in the field as such. "Medically assisted reproduction" is a strange term that, to a lay person, could be interpreted as representing the act of reproduction since it is used here as a noun, as opposed to the very commonly used "assisted reproductive technology". "Oocyte Pick-up" is also strange. Pick-up is used in place of "trucks" in the states.	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table, With regards to the other terms, we have followed previously published and internationally used terminology (ICMART) and previously published ESHRE documents.,
M.H.Mochtar	6	45	women with (…) and with (…) must be OR	This was corrected in the text,

Linda Giudice	6	46	Spelling of "lose"	This was corrected in the text,
BLEFCO	8		Is it possible to add the meanings of "GPP" and "GDG" in annex 2?	This was added to the text wherever relevant
GGOLFB	9	16	Need to define SLE	This was corrected in the text,
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	7		The list of all recommendations: The questions in the headings are not actually answered by the compiled recommendations at each point. Should the questions be replaced by simple headings? The recommendation sentences could be reviewed and overlapping statements clarified.	We have double checked the headings for consistency and modified where needed. We also revised the final list of recommendations and rephrased where appropriate
BFS	5 and 163	18 & annex 4	Scoping selection of your 21 key questions is comprehensive and useful	Thank you!
Gareth Greggains	7-15	1-78	This is a very well structured and thorough guideline. We hope that the final draft will include the 'list of recommendations' on pages 7-15 since this provides healthcare professionals with an overview or quick reference area prior to or after reading the guideline in its entirety.	Thank you for this comment. We will include the list of recommendations as it currently is available in the draft,
Shelley Grant	Cover	Sub-title	Replace "Guideline of … " with, "A Guideline for Clinical Support from the European Society for Human Reproduction and Embryology"	Our guidelines have a standard cover and standard disclaimer. We decided not to adapt this.
Linda Giudice	general		Like all guidelines, some recommendations will have a short lifetime and some may be controversial in different parts of the world However, outstanding effort.	Thank you!
M.H.Mochtar	general		I have some (minor) comments on this very nice and high quality guideline.	Thank you!
Eleftheria Kourenta	general		*General Comment:* The document is patient-friendly and take under consideration patient needs.	Thank you!
Linda Giudice	general		Overall this is an outstanding document on female fertility preservation. Just a few items:	Thank you!
Linda Giudice	general		I was not clear about whether the reader would realize that evidence for endometriosis patients would be included in this document as they do not appear to fall in the 4 patient populations listed	This is a fair point, and consequently, we added some clarifications in the introduction and throughout the guideline (under 'benign diseases').
Linda Giudice	general		Also, while this is devoted to female FP, perhaps a comment about male fertility preservation could be made in the introduction – just to emphasize the issues as especially as most young men, Men with testicular cancer are usually not	Agreed, We have added a sentence on male fertility preservation in the guideline introduction,

			referred for sperm banking by oncologists or urologists unless they are particularly aware of the potential of fertility loss with treatment.	
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	general		Throughout the text there is a general idea that fertility preservation measures should be performed when there is a risk of cytotoxic treatment. Except for ovarian tissue cryo, there is no discussion whether the measures would be OK AFTER the start of the cytostatic treatments. The statement should include a clearer stand on this matter.	This aspect is discussed in the introductory chapter (Part A 'Second phase of fertility preservation (after cancer treatment)).
Ira Winter	general		The philosophical starting point of this draft document is not the desire for full fertility restoration, but to advance the best IVF/ART practice. One must scroll to page 96 to read about 'an alternative' to egg freezing. Yet only techniques such as ovarian wedge freezing Wedge freezing allow for the possibility of natural conception after re-implantation. Medicine will progress where resources are invested. Fertility preservation does not start or end with the baby. The whole experience of female fertility potential is worth preserving and fighting for. Preserving. By not putting fully restorative techniques in the first place and other techniques as alternatives later, resources will be channeled according to most exciting medicine and away from what patients really want, if asked. Any argument that egg freezing is more effective is based on past and current resources and efforts having been channeled in that direction. If the authors of this document reversed the order of presentation it would go a long way towards highlighting what is possible and give a greater chance that future resources would be given towards perfecting techniques that also preserve the Natural conception potential in the future of the patient.	The scope of the guideline is fertility preservation, being to enable women to achieve parenthood after gonadotoxic or other treatment. Optimisation of female reproductive potential is included where relevant, but this was not the aim or the focus of the current guideline. It was decided not to reverse the order of the sections.
Eleftheria Kourenta	general		General Comment: For the cancer patient point of view, it would be better a guideline focused only on cancer patients	The scope of the guideline, as decided at the start of the project, included fertility preservation for different patient populations, and this required a broader remit.
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	general		The title "Fertility preservation" should be reviewed, as in effect, gametes and gamete-containing tissue are preserved, not fertility per se. This should be also discussed in the text (eg. ref. Grynberg and Sermondade, Human Repr 2019: 34; 1855-1857).	We recognise this, however 'fertility preservation' is the widely used and accepted terminology
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	general		In the guideline, sexuality issues are largely ignored. Ethical aspects, informed consent, overall awareness of fertility preservation options could also be discussed in more detail.	We respectfully disagree, and have endeavoured to include all these topics in this guideline. We recognise that all could be covered in more depth, but given that this guideline is already very long (and considered to be too long by some),

Oncofertility Consortium	general		There is no scientific reason to eliminate the term 'oncofertility' and replace it with 'FP in cancer patients'. For the purpose of continuity of the literature, there is no reason to place the term outside of the acceptable terminology grouping. Oncofertility is an established field of medicine and by eliminating it from acceptable terminology, you will lose a substantial amount of literature and awareness among providers and patients.	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table,
John Tzafetas	general		The terms: Oncology and Fertility traditionally have been the terms representing the two relevant subspecialties of: i. Oncology/Cancer and ii. male/female Fertility/subfertility and this is how they have been established The newly introduced term 'Oncofertility' includes, in one word, both these fields adequately. Apart from being elegant, it is short and practical and does not include the rather unpleasant word 'cancer'. For these reasons, I believe, the term 'Oncofertility' is more advantageous.	The guideline group decided that for this project, describing recommendations for 4 different patient groups, using 'fertility preservation' and "fertility preservation for cancer patients" where specific for oncology patients is most appropriate. However, this does not mean that the guideline group suggests the term oncofertility is not acceptable, We understand the table on terminology could give the wrong impression and we have decided to delete the table,
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	general		The writers do not give any recommendations on the desired number of frozen oocytes (/ embryos) per patient; 10-15 oocytes?	There are only a few reports on the use of stored oocytes for establishing pregnancy. We clearly describe how the chance of pregnancy is dependent on the number of oocytes frozen, and the woman's age. As such, there is no 'optimal' number of oocytes that should be stored: it will depend primarily on the woman's response to OS. It was decided not to include a recommendation on this.
Carlos Calhaz-Jorge	general		Congratulations to the authors of this superb Guideline! However, I feel that some sections are a little too long and could be shorten without losing their value (i.e., Parts A and B, but some more subsections) An important number of so-called Recommendations do not follow the expected format and are really statements, albeit important. Please check Recommendations 8, 12-18, 20, 27, 28, 34, 46, 48, 53, 54, 63 and 72 listed in pages 8 to 15	Thank you for this comment. We have assessed the listed recommendations and whenever possible, we changed them to the format of a recommendation.
Eleftheria Kourenta	general		General Comment: There is no definition for GPP	The full term "Good Practice Point" was added in the text and in the list of abbreviations
Working Group for Reproductive	general		Pages 2-4 Table of contents and the structure of the paper are not logical, f.ex. Elective oocyte cryopreservation is under C3 Ovarian reserve testing, Effect of	We have double checked the headings for consistency and modified where needed. The latter

Endocrinology of the Finnish Society of Obstetrics and Gynaecology			age is only mentioned under embryo cryo. Consent and counselling are only mentioned in oocyte non-medical reasons cryo.	issue on counseling is specifically included in the section on non-medical FP, general counseling is included at the start of the guideline
Carlos Calhaz-Jorge	general		Congratulations to the authors of this superb Guideline! However, I feel that some sections are a little too long and could be shorten without losing their value (i.e., Parts A and B, but some more subsections). An important number of so-called Recommendations do not follow the expected format and are really statements, albeit important. Please check Recommendations 8, 12-18, 20, 27, 28, 34, 46, 48, 53, 54, 63 and 72 listed in pages 8 to 15	Thank you for this comment. We have assessed the length of the document and we don't think it is too long. Condensing it further will eliminate relevant and helpful information. The list of recommendations at the start of the project should help professionals interested in the recommendations, but not in all the background information.
GGOLFB	general		Congratulation for this wonderful work!	Thank you!
BFS	General		Congratulations to the guideline development group and to the ESHRE staff for the huge amount of careful work undertaken to produce this excellent guideline	Thank you!
Monica M Laronda	Title, summary and Throughout		"Female" is used throughout this document where we may also want to include fertility preservation for transgender men. I would consider revising "female" to "individual" or "individual with ovaries" where appropriate to be inclusive of the sections on Transgender Men.	The guideline group attempted to be inclusive by including the 4 different populations, and transgender men. The documents title was also formulated to be inclusive. Changing it to "'individuals with ovaries" would probably not be appropriate for the 3 other patient groups.
E.E.L.O.Lashley			First of all we would like to thank and compliment the committee with finalizing this guideline. The document represent a good and complete overview of all recommendations. Beneath you can find our comments. Please contact us if anything is unclear	Thank you!
A1. Organisation of care				
E.E.L.O.Lashley	7		The figure on organization is somewhat unclear with the use of different colors of the letters, different sizes of the arrows etc In addition, we would suggest that the 'fitness for pregnancy' question is the most important question in this period. We would therefore suggest that this question is placed directly under the AFTER TREATMENT. Also, in the clinical care team confronted with this 'fitness for pregnancy' question an obstetrician should be involved, next to the oncology team and gynecologist.	During stakeholder review, we have updated all figures.

Shelley Grant	16	36 (A1)	Replace "Multidisciplinary Team Approach" with, "Outlining a Team Approach to Care". Then, substitute the term "multidisciplinary" in later sections (e.g. T with "care team"	The term "multidisciplinary" is used to emphasize the connection of the different clinical care teams with the FP team. We have adapted the heading as suggested.
Shelley Grant	16	7	Replace the current introductory sentences (starting with "This guideline …") with, "This guideline aims to help providers meet a growing demand for FP options by a diversely interested patient categories. Significant research establishes the need to inform patients responding to cancer or various benign diseases about the impact of undergoing gonadotoxic treatment on their fertility health. This adds to a need to support clinician efforts to address the growing interest in FP options among healthy females and transgender patients."	We have included some of these ideas from the suggested text.
Shelley Grant	16	44 (A1 org of car e)	Re-phrase the sentence starting "A dedicated … " to read, "Studies indicate the addition of a psychologist or counsellor dedicated to improving communications between doctors and patients can positively impact the emotional experience and decision making capacity of care recipients."	We have rephrased this sentence.
BFS	19	84	The BFS is delighted to see your recommendation on fertility education	Thank you!
Shelley Grant	19	61	Replace. "Steps to Overcome barriers to fertility preservation" with, "Expanding Access to Fertility Preservation Options". Motivation: The language in the original phrasing is predictive and implies that process delays or caps on care-seeking are aimed at restricting care access. The original language excludes the possibility that many rules variously aim to protect patient interests in care contracting and reduced exposure to health risks.	we have adapted the heading as suggested
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	20	112	Page 20 Line 112- and page 22 line 187. Adolescents are discussed twice.	We merged the information on adolescents in 1 section,
M.H.Mochtar	21	159	One should be aware of gender dysphoria (which is mentioned later on) during the IVF procedure in transmen I therefor like to recommend to seek contact with the transgender team who has guided the transman in his transition.	We agree with this comment, and have added some information in section D to address this comment
BFS	21	146	Should the guideline include fertility preservation in pre-pubertal and peri-pubertal females?	In the introduction of the guideline we explain that the guideline specifically focusses on post pubertal women. We have clarified this further in the section "patient population"

Shelley Grant	21	143 to 147	Include an in-text reference to similar work by Hirschfeld-Cytron et al. 2012 (fully citated below), which estimates the changes to FP care patterns caused by a primary reliance on cost-benefit evaluations for decisions on care type and timing. The current document fails to detail the clinical needs to support patients seeking to form or execute long-term family planng strategies, especially among sub-categories of sponsored younger and/or highly informed elective FP candidates. Hirshfeld-Cytron J, Grobman WA, Milad MP. Fertility preservation for social	We have checked the paper, but decided not to refer to it. It is about a model calculation cost effectiveness of FP for non-medical reasons for women planning delayed childbearing: comparing oocyte freezing at age 25, ovarian tissue at age 25 or no FP the age of 25 and waiting for spontaneous pregnancies up to the age of 40. The conclusion was that it is cost effective to do nothing at the age of 25.
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	21	160	Page 21, lines 160. We suggest to rephrase the text more clearly that the effects of long-term gender-affirming hormone therapy on ovarian function / fertility is not known. Therefore, the real need for fertility preservation is unclear.	In the referred section, the need for a discussion on FP is mentioned, not the need for any interventions. With regard to interventions, the guideline clearly states that "patients require an individual assessment of the indications and risks prior to fertility preservation interventions"
Carlos Calhaz-Jorge	21	152	"be frozen. This is discussed in more detail in chapter D6. Ovarian tissue cryopreservation but". Please, delete the last word ("but").	This was corrected in the text,
BLEFCO	22	194	The use of new technologies (website, applications, etc.) for educational materials may be mentioned in the specific care of young patients.	We have revised the sentence and decided not to go into detail in part A. Part B includes more information on information provision.
GGOLFB	22	192	FP and not FO	This was corrected in the text,
BLEFCO	22	192	It seems there is a mistake: "FO" may be replaced by "FP"	This was corrected in the text,
BFS	22, 23	200 , 207	Consider ethical concerns when an <16's wishes conflict with parents	We added a sentence at the end of the paragraph reading 'This might give rise to ethical concerns in case of conflicting wishes.'
M.H.Mochtar	24	233	I miss that women should be aware that, when they return to use their stored eggs, a psychosocial screening is mandatory (mentioned later on in the guideline: welfare of the child)	Although this aspect was discussed later on in the guideline, and obvious (because it is normal practice for all fertility treatments, we still added a sentence.
M.H.Mochtar	24	233	Clinics should be prepared to perform shared lesbian (in this case transgender) motherhood or surrogacy when they store eggs of transmen, since transporting frozen egg to another clinic is not without risk.	We have assessed this comment, but decided not to make any adaptations to the text.
BLEFCO	24		Patient's "serology" may be replaced by patient's "serologies" since the multiple serologies applied in some countries (HIV, HBV, HBC, ..)	We have not put more details on serological testing as this may differ between countries, but "patient's serology" is correct from a linguistic perspective,

				meaning one or more serological tests. We have not modified this.
A2. Legal aspects and availability + A3. Storage of reproductive material				
GGOLFB	26	22	"cryopreservationis » a space is missing	This was corrected in the text,
Carlos Calhaz-Jorge	26	7	Embryo cryopreservation for FP is also allowed in all countries except for Italy and Portugal	This was adapted in the guideline.
Carlos Calhaz-Jorge	26	17-19	Please consider that in Portugal patients may have FP without costs under the NHS but must pay if choose to go to a private centre.	We added the information on Portugal
Gareth Greggains	26	26	Norway – it is now legal to cryopreserve oocytes, embryo or ovarian tissue in benign disease.	This was adapted in the guideline.
Gareth Greggains	26	27	Norway – the costs of procedure are reimbursed	This was adapted in the guideline.
Gareth Greggains	27	49	While surrogacy is still illegal, Norway now allows partner donation of oocytes by transgender men.	We have corrected the sentence to make sure the information on Norway is correct.
Dr. Bettina Böttcher/ Prof. Dr. Bettina Toth	28	3	Austria: Embryo cryopreservation and ovarian tissue cryopreservation: provided without costs: NO , for ovarian tissue one could add the footnote "8": storage fees	This was adapted in the guideline.
SGGG	28	64-65	Table 1 Fertility Preservation options for cancer patients (per country) and information on the costs for patients. In Switzerland, since 01.07.2019, cryopreservation of mature oocytes and ovarian tissue are covered by the health insurance (obligatory for all Swiss citizen) until the 40th birthday when the risk of amenorrhea induced by the gonadotoxic treatment is >20%. Fertilisation of oocytes for embryo cryopreservation is not covered.	This was adapted in the guideline.
Margarita Chrysanthou Piterou	28	64-65	There is no data from Greece for these FP options. Is there any way to find and add some? As I understand from Annex 6 (page 167), there was no reply to your survey form national representatives. However, there is some literature that you can rely on, for example: Leon G, Papetta A, Spiliopoulou C (2011) "Overview of the Greek legislation regarding assisted reproduction and comparison with the EU legal framework", Reproductive BioMedicine Online, 23(7): 820-823.	Data were collected through the ESHRE committee of national representatives. Unfortunately, we did not receive any data on Greece. As the published report is from 2011 and we could not verify whether the data is still up to date, it was decided not to add the information on Greece.
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	28	table 1	Finland: All options (Oocyte, Embryo, Ovarian tissue cryo) are allowed, but not provided without any costs (Reimbursement partly)	This was adapted in the guideline.

Dr. Bettina Böttcher/ Prof. Dr. Bettina Toth	29	3	Austria: footnote 1 is wrong as no specific indications are provided in the law. Please change Change to "medical indication needed"; same applies for footnote "6": no specific Indication is provided, "medical indication needed" would also apply Austria: Embryo cryopreservation: provided without costs: NO, for ovarian tissue one could add the footnote "8": storage fees	This was adapted in the guideline.
SGGG	29	68/ 69	Table 2 Fertility Preservation options for patients with benign diseases (per country) and information on the costs for patients. information on the costs for patients In Switzerland, starting 01.07.2020, cryopreservation of mature oocytes and ovarian tissue are covered by the health insurance (obligatory for all Swiss citizen) until the 40th birthday when the risk of amenorrhea induced by the gonadotoxic treatment is >20%: selected cases: only in selected cases: stem cell transplantation or cyclophosphamide therapy when the risk of amenorrhea is >20%. Fertilisation of oocytes for embryo cryopreservation is not covered.	This was adapted in the guideline.
Gareth Greggains	29	69	Norway: oocyte cryopreservation: allowed; without costs for patients: yes embryo cryopreservation: allowed; without costs for patients: yes ovarian tissue cryopreservation: allowed; without costs for patients: yes	This was adapted in the guideline.
Margarita Chrysanthou Piterou	29	68-69	There is no data from Greece for these FP options. Is there any way to find and add some? As I understand from Annex 6 (page 167), there was no reply to your survey form national representatives. However, there is some literature that you can rely on, for example: Leon G, Papetta A, Spiliopoulou C (2011) "Overview of the Greek legislation regarding assisted reproduction and comparison with the EU legal framework", Reproductive BioMedicine Online, 23(7): 820-823.	Data were collected through the ESHRE committee of national representatives. Unfortunately, we did not receive any data on Greece. As the published report is from 2011 and we could not verify whether the data is still up to date, it was reluctantly decided not to add the information on Greece.
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	29	tab kle 2	Finland: Benign indications are accepted (All options (Oocyte, Embryo, Ovarian tissue cryo) are allowed, but not provided without any costs (Reimbursement partly).	This was adapted in the guideline.
Gareth Greggains	30	72	Norway: oocyte cryopreservation: allowed; without costs for patients: yes embryo cryopreservation: no; without costs for patients: no ovarian tissue cryopreservation: not allowed; without costs for patients: not applicable	This was adapted in the guideline.
Margarita Chrysanthou Piterou	30	71-72	There is no data from Greece for these FP options. Is there any way to find and add some? As I understand from Annex 6 (page 167), there was no reply to your survey form national representatives. However, there is some literature that you can rely on, for example: Leon G, Papetta A, Spiliopoulou C (2011) "Overview of the Greek legislation regarding assisted reproduction and comparison with the EU legal framework", Reproductive BioMedicine Online, 23(7): 820-823.	Data were collected through the ESHRE committee of national representatives. Unfortunately, we did not receive any data on Greece. As the published report is from 2011 and we could not verify whether the data is still up to date, it was decided not to add the information on Greece.
Working Group for Reproductive Endocrinology of	30	tabl e 3	Finland: All options (Oocyte, Embryo, Ovarian tissue cryo) are allowed, but not provided without any costs (Reimbursement partly).	This was adapted in the guideline.

the Finnish Society of Obstetrics and Gynaecology				
Gareth Greggains	31	77	Norway – FP for non-medical reasons is now legal. The patient must pay full costs of treatment.	This was adapted in the guideline.
verena Nordhoff	33		For page 33 please add for duration of storage: „no limit“ and „defined by clinic“, and for age limit for use: „recommended maximum age <50y“. - Germany	This was adapted in the guideline.
Gareth Greggains	33	107	Norway – oocytes, embryos and ovarian tissue can be kept until the patient's 46 year of age.	This was adapted in the guideline.
BLEFCO	33	FRANCE	In France, current practice of stored material for oocytes and embryos is 45 year	This was adapted in the guideline.
BLEFCO	33		In France, the age limit for the use of ovarian tissue is not defined. Could you correct in the table 5?	This was adapted in the guideline.
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	33	Table 5	Finland: All options: Limited, defined by clinic, age limit defined by clinic, up to 50 years.	This was adapted in the guideline.
Miguel Moreno	34	4	I would like to explain that there is some wrong information on page 34. There is no limit in connection with the “age limit for use of stored material” in 40 year. There is no maximum limit in the Spanish regulation, more that “until the woman is not in conditions of receiving an ART” (Spanish clinics agreed until the age of 50 years old).	This was adapted in the guideline.
verena Nordhoff	28,29,30		Page 28, 29 and 30 For Oocyte cryopreservation, Embryo cryopreservation and Ovarian tissue cryopreservation you can add „allowed“ and that it is provided with costs for the patients (meaning NO). Germany	This was adapted in the guideline.
Dr. Bettina Böttcher/ Prof. Dr. Bettina Toth	30-33-122	3	could add a footnote “8”: storage fees Austria: Transgender: ovarian tissue allowed Austria: Ovarian tissue: limited storage, lifetime	This was adapted in the guideline.
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	table 1		Table 1: In Finland Embryo cryopreservation and OTC are allowed, too. All treatments (OC, EC, OTC) are partially reimbursed.	This was adapted in the guideline.

Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	table 2		Table 2: OC, EC and OTC are allowed in Finland. Please, exclude "not performed", since these treatments are performed. The treatments are partially reimbursed.	This was adapted in the guideline.
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	table 3		Table 3: (V), (meaning allowed under conditions) appropriate for Finland, partially reimbursed. OTC – (not performed). Please, exclude footnote 2.	This was adapted in the guideline.
Carlos Calhaz-Jorge	Table 5	Portugal	Embryo cryopreservation for FP is not allowed in Portugal. The information presented in the table refers to embryo cryopreservation resulting from infertility treatments. So, I think it should be deleted from the table	This was adapted in the guideline.
Carlos Calhaz-Jorge	Tables 1, 2 and 3	Portugal	Oocyte cryopreservation - Provided without costs for patients: Yes, under the Health National Service; No, if the patient choice is to go to a private centre	This was adapted in the guideline.
Shelley Grant	32	84-86 A3	The Table 5 (pp.33-34) display of national rules is well-presented and informative. Yet, this summary of national tissue storage policies would benefit from brief supplementary descriptions on other factors concerning storage decisions, such as 1) patient election to store reproductive cells or tissues at a facility situated outside of the primary country of residence, based on independent motivations or the suggestions of medical advisors. There is, to my knowledge, little knowledge on the association between storage restrictions and geographical patterns in storage, and 2) the impact of changes to interpretations (original or revised) on the regional European Tissues and Cells Directives legislation on patterns of storing reproductive materials (Directive 2004/23/EC and Directive (EU) 2015/566)). Such changes may also result from the2019 Evaluation of EU blood, tissues and cells legislation, conducted under the regional public health provisions European Centre for Disease Prevention and Control (ECDC) to improve earlier legislation, and 3) efforts to prevent the spread of COVID-19 are likely to include amendments to current storage rules detailed above. Such concerns are patterned off of earlier and ongoing efforts to avoid cross-contamination in storage with HIV, Ebola, West Nile and Zika viruses (ECDC). This adds to very recent studies on the potential heritability of antibodies, a further motivation for stricter tracking and monitoring of stored materials. These are three of many possible considerations on storage that arguably belong among the recommendations in this guideline and address a gap in knowledge on a factor for FP success.	These are important issues but largely research questions. We hope that providing this information will act as a catalyst to promote the development of these issues.

Gareth Greggains	32	103	Incorrect spelling of the word countries.	This was corrected in the text,
BFS	33	106	Ditto, this survey provides powerful data to influence national regulations on storage periods	We agree and hope this overview will indeed help to improve national regulations, We already mentioned the variability in the conclusion, and consider it not necessary to further expand on this.
B1. Information needs and provision + B2. Support and counselling				
BFS	29	64	The table confirms considerable variation in provision and funding across Europe. Perhaps ESHRE has a role at European level in promoting equitable provision of services?	We agree and produced this table as a starting point towards that, along with data collection by the ESHRE IVF monitoring.
Margarita Chrysanthou Piterou	36	62	Recommendations: Information about birth outcomes and long-term follow-up of the children born after treatment could be included, because patients highlight the importance of having material to support their decision.	We agree that this is important. As detailed in the table, information on pregnancy after gonadotoxic treatment or underlying condition includes "Effects of disease/treatments on future children", which includes information on birth outcomes and long term effects . We decided no further addition was needed.
E.E.L.O.Lashley	8	1	Change: 6) pregnancy after cancer into: pregnancy after gonadotoxic treatment or underlying condition Commentaar: individuele afweging welke vorm van FP meest geschikt is voor pte	We have changed the sentence as suggested,
BLEFCO	36	54-57 and 58-61	The paragraph is duplicated	This was corrected in the text,
Eleftheria Kourenta	40	231	The recommendation for the use of a checklist it would be better to be STRONG	The evidence on the effect of this checklist is small and weak. With regards to the recommendation for using the checklist, we consider it appropriate to label it as a weak recommendation. The need and usefulness of a checklist depends on expertise of the practitioner. We do not want to recommend the use of the checklist for everyone, but rather for those who might need it. We have not adapted the recommendation.

BFS	44	310	Psychologists/counselors for FP: fertility counselors? TYA counselors? Oncology counselors? Multi-professional approach? What kind of training should FP counselors have?	As referred in the text, fertility counselling refers to the provision of information regarding infertility risks and FP options. This is usually performed by a specialist in reproductive medicine, supported by a multidisciplinary team that addresses the clinical situation of each patient. psychological counselling is targeted at exploring reproductive concerns and promoting strategies to deal with the stress of the decision in the short and long term. This type of counselling should be provided by someone with professional background and training in psychosocial counselling.
GGOLFB	45	334	"survivorsreproductive" a space is missing	This was corrected in the text,
Carlos Calhaz-Jorge	42-Checklist 2		It is strange that in transgender men "Effects of hormonal stimulation for FP on disease recurrence" is considered a possibility (marked as √)	We have corrected this in the guideline.
C1. Patient selection				
BFS	48	27	Suggest to discuss mediastinal masses as Hogdkin's lymphoma forms a large group referred for FP	We agree with this comment and have added "mediastinal masses" to checklist 3,
BLEFCO	48	7-9	This sentence suggests that some patients may not need fertility preservation although it is currently difficult to state with absolute confidence that these patients won't be infertile. Could you reformulate this sentence?	We added a sentence added at the end of the paragraph, reading "Importantly however there remains uncertainty over the risk when applied to an individual."
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	48	3	Patient selection: Preferences, number of children, social status and local resources should be mentioned.	We have modified the table based on this and other comments, It now includes "availability of local resources, expertise and local criteria/funding ".
BFS	49	48	Risk of haemorrhage in thrombocytopaenic, pancytopaenic patients (including aplastic anaemia who require BMT)	We agree with this comment and have added the suggested sentence,
BFS	8, 50	Rec 8, 52	Wording of recommendation "the need and suitability of FP", "need" may not be the correct English word here – no one "needs" to do FP, it is an individual decision. Suggest "indication and risks"	We agree and have corrected "needs and suitability" to "indications and risks"
C2. Gonadotoxic treatment				

GGOLFB	50	26	Shouldn't we add the notion that often these patients are on contraceptive and therefore there is an impact on hormone dosages, even AHM?	We have addressed this issue in the section on ovarian reserve testing, by adding a sentence on the possible impact of contraceptives.
E.E.L.O.Lashley	50	8	Change: "anticancer" into gonadotoxic	We have adapted "anticancer" to "gonadotoxic" throughout the guideline
Carlos Calhaz-Jorge	51	49	"crucial factor, for which the evidence has been discussed in section C3." Maybe better to "will be discussed" because section C3 will follow	This was corrected in the text.
Margarita Chrysanthou Piterou	52	121	Please, indicate if this negative effect exists also in healthy carriers of germline BRCA mutations.	We have modified the paragraph including information on healthy *BRCA* carriers.
M.H.Mochtar	55	199	Gynaecological cancers: can the committee share their considerations on FP in patient with cervical cancer is there a place for an abdominal approach or should we stick to transposition or ovarian tissue preservation?	This is a relevant comment, but fertility sparing surgical interventions were considered outside the scope of the current guideline. As such, this was not addressed in the guidelines.
BFS	55	236	Gynaecological cancers: Role of oocyte cryo-preservation in borderline ovarian tumours (especially recurrent borderline ovarian tumours) Atypical hyperplasia and endometrial cancer: waiting for tumour regression and natural conception: any role of IVF with cryo-preserved oocytes or embryos due to time factor	This is a relevant comment, but this topic is considered outside the scope of the current guideline.
GGOLFB	56	266	94.1% risk of amenorrhoea but for how? Woman older than 40 years? why isn't that in the table7?	This aspect is included in the table as "radiotherapy that include the ovaries".
Carlos Calhaz-Jorge	Section C.2	51-57	I feel it is too long and detailing an excessive number of small studies. The bulk information is presented in Table 7. Could the section be condensed?	The evidence behind the table is outlined in the text and we think it is relevant to keep this information, as it is a key part of the evidence needed to properly counsel patients. The summary tables and recommendations can be quickly checked if the reader does not want to go into too many details in the text.
E.E.L.O.Lashley	9 and 59	10 and 378	Change: "In all patients undergoing anticancer treatments into: in all patients undergoing gonadotoxic treatments	This was adapted as suggested.
C3. Ovarian reserve testing				
Hanna Savolainen-Peltonen, Eini			There is inconsistency between #20, page 9 and #38, page 11. The limit for OTC is rather low – would it be clearer to use the same AMH/AFC threshold for low ovarian reserve?	We have adapted the threshold for AMH to 0.5ng/ml in all recommendations

Nikander, Varpu Ranta				
Carlos Calhaz-Jorge	63	03/04	"ovarian functionality at a given point in time (Iwase *et al.*, 2014). Ovarian reserve status is related to response to ovarian stimulation and reduced fertility and can be a useful surrogate marker for". Ovarian reserve *per se* is not related to reduced fertility. I suggest "to ovarian stimulation and fertility potential" instead.	The sentence was adapted as suggested by the reviewer
Gareth Greggains	63	21	Consider also under the PICO question on line 21, whether pretreatment AMH is relevant with regards to comparing ovarian reserve pre and post chemotherapy or SCT treatment'. If there is evidence, then it would be useful to include it as a recommendation on page 64. It would as a minimum provide useful information to the patient.	We agree with this comment, but it is largely relevant to post cancer care, We added a sentence in the text.
BFS	63	21	Discussion on difficulties of interpretation of AMH in very young post pubertal girls, individuals on hormonal contraception	We added a sentence to the text in reply to this comment reading " It is important to recognise that there may be differences in interpretation of ovarian reserve testing in adolescents compared to in older women, and that there is an impact of taking hormonal contraception. "
BLEFCO	63	42	The reference of Grynberg et al., 2019, may not be appropriate with the idea. It could be better to mention the publication of Sermondade et al., 2019 (reference page 119, line 248)	We have checked and adapted the reference in the text
Carlos Calhaz-Jorge	63	6	Ultrasound is not really "radiological". Suggest "imaging" instead.	This was corrected in the text,
Carlos Calhaz-Jorge	64	73	Recommendation is about "estimation of risk" and partially repeats the last recommendation of previous section. Why not to consider "pre-treatment AMH levels" here (patient and treatment characteristics were already considered)?	We agree with this comment, but reading the justification, it was formulated to clarify that one should not use AMH alone. We have slightly changed the wording of the recommendation to clarify this
Aboubakr Mohamed Elnashar	10	20	A clear cut for reduced ovarian reserve is important, not a range. It should be less than 0.5 ng/ml for AMH	We have corrected this to a threshold for AMH of 0,5ng/ml rather than the suggested range.
Carlos Calhaz-Jorge	65	109-111	The sentence "Although menstrual irregularities are associated with the disease activity (Shabanova et al., 2008), no correlation was found between AMH levels and disease activity (Lawrenz et al., 2011)." is a little tricky. It suggests that there exists a known correlation between menstrual irregularities and AMH levels, which is not the case. Maybe delete the first part of the sentence and keep "no correlation was found between AMH levels and disease activity (Lawrenz et al., 2011)."	The sentence was adapted, similar to what was suggested by the reviewer,

Stephan Gordts	66	143	Endometriosis - Concerning oocyte cryopreservation the refence of last publication of Cobo et al in Fertil Steril can be added, Negative impact of endometrioma in adolescents is clearly demonstrated in study of Nieweglowska Reprd Biol and Endocrin 2015:13-128	The deadline for inclusion of studies was 1 November 2019, and hence the study by Cobo was not picked up in our literature review. As the study does not show any new data that would require an update of the recommendation, it was decided not to include it. We include a large and recent meta-analysis (highest quality of evidence), and as such the Nieweglowska paper was considered lower quality of evidence without adding additional information.
GGOLFB	66	138	"Error! Reference source not found" and same line: "treatment"	This was corrected in the text,
Carlos Calhaz-Jorge	67	193 - 196	The sentence "Substantial evidence from several studies demonstrates that low AMH levels and other biomarkers of ovarian reserve are affected … or by medical interventions (such as gender reassignment surgery)" sounds strange. I suggest to delete the word "surgery" because I guess the authors refer to a decrease of the ovarian reserve linked to a previous long-lasting hormonal treatment. Of course ovarian reserve will become zero after oophorectomy.	Thanks for spotting, the word 'and' was missing before surgery. We have corrected this and slightly rephrased the sentence.
Carlos Calhaz-Jorge	67	201	The recommendation "**For women with overt POI, fertility preservation is not recommended"** would not be better located in section C1.? In fact, it is a general statement and not directly linked to the Ovarian reserve testing	We agree and have moved the recommendation to section C1,
Alexandra Kohl Schwartz	67	144	Suggestion for insertion of the following sentence: "approximately 40-50% of young women experience a recurrence of endometriosis before trying to become pregnant (Brosens et al. Hum Reprod 2013). In these cases, fertility counseling is absolutely essential",	In the current guideline, the focuss was very much on fertility preservation, Endometriosis recurrence will be covered in the ESHRE Guideline on Endometriosis,
Alexandra Kohl Schwartz	67	161	Suggestion for insertion of the following sentence: " Mechanical stretching of the ovarian cortex by endometrioma leads to increased ovarian fibrosis and reduced follicle density (Kitajima et al fert steril 2011)" (after "evident")	In the current guideline, the focuss was very much on fertility preservation, other endometriosis topics will be covered in the ESHRE Guideline on Endometriosis.
Carlos Calhaz-Jorge	69	221	Recommendation (as in (The ESHRE Guideline Group on Ovarian Stimulation *et al.*, 2020)) I guess this is a general recommendation but it follows a subsection "Elective oocyte cryopreservation" whose last sentence states that "ovarian reserve testing should not be measured for making FP decisions". Maybe the format and/or location of this general recommendation can be improved. Just to avoid misinterpretation	We agree and have inserted the recommendation in the introduction of the chapter
D1. Options for FP				

BLEFCO	74	Fig 4	Surrogacy is not allowed in all European countries . An asterisk may specify "if permitted"	We have adapted the figure in reply to this comment,
E.E.L.O.Lashley	74	29	In the figure it seems as if GnRHa protection is a first option within fertility preservation, while it is clearly stated that GnRH agonists during chemotherapy should not be considered an option for fertility preservation instead of cryopreservation techniques. We would suggest to adapt the figure so this is more clear.	We have adapted the figure to accommodate this comment, specifying GnRHa as a separate option.
D2. Ovarian Stimulation in treatments aimed at FP				
BFS	75	1	Should VTE risk assessment and LMWH during ovarian stimulation in cancer/SLE etc be addressed?	We recognised this is an important topic, and thrombotic risk is covered in the section on patient assessment prior to FP interventions. We did not find relevant evidence in the literature search, thus it is not discussed more fully.
Carlos Calhaz-Jorge	76	44	Recommendation - "weak" strength - Some lines below: *For non-urgent ovarian stimulation, the planning of cycles using GnRH agonist protocols is feasible and could be used if preferred, as a good practice point (GPP)* It looks inconsistent. Maybe just my incorrect interpretation.	We corrected the justification, there was indeed an inconsistency,
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	10	23	#23, page 10 we suggest to rephrase "The use of a long protocol may also be appropriate", since the use of an antagonist protocol is appropriate in this situation, too.	We have adapted the recommendation as suggested
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	10	24	Page 10 Line 24 and page 76 line 44 The conclusion gives the impression that the long protocol would be preferred here, despite the text (p 76 line 51-) stating that it COULD be used.	This was adapted based on another comment
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	10	26	Tamoxifen could be discussed despite less information (Page 75 line 40, page 78 line 158-), preferably to encourage further studies.	We decided that we should not expand on the evidence for tamoxifen co-administration, but we added a statement on the requirement of further research on the topic.
Carlos Calhaz-Jorge	77	93	Recommendation - I suggest to delete the word important. As stated in the Justification paragraph the follows, data is not yet robust	We agree with this comment and have deleted the word "important"

Stefan Matik	77	93	If the patient is around the time of ovulation, aspiration of the follicle could be considered in an attempt to obtain an oocyte, before initiating the random-start ovarian stimulation	We assessed this comment but decided this is not an established procedure and as such it should not be added to the guideline.
Stefan Matik	78	141-142	Co-administration of aromatase inhibitors might also be considered after the OPU, not only during ovarian stimulation, i.e. before the OPU, if estradiol levels 3 days after the OPU are above a certain value (e.g. >250 pg/mL, until they decrease to <50 pg/mL).	We have added the following sentence at the end of the paragraph: Co-administration of aromatase inhibitors may be restarted and maintained for a few days after oocyte retrieval, aiming at further reducing systemic estradiol levels (Oktay et al., 2010).
BLEFCO	78	158 - 159	"the numbers of oocytes retrieved of mature oocytes…" may be confused. It could be replaced by "the number of mature oocytes retrieved"	This was corrected in the text,
BLEFCO	78	164	"Stimulatiion" has to be replaced by "stimulation".	This was corrected in the text,
GGOLFB	79	188	I think you should indicate the dose of letrozole to be used	We added the dose of letrozole used in the study of Marklund in the text.
BFS	79	196	Transgender men find menstruation distressing. Discussion about whether withdrawal bleeding is necessary prior to stimulation or it can be avoided by shortening the testosterone free interval. Also withdrawal bleeding after egg collection can be reduced by starting or restarting testosterone soon after egg collection?	We have described the evidence according to the literature, and to our knowledge, there is no evidence so far to include the suggestion regarding a withdrawal bleed. We did however add a sentence reading: "Avoidance of menstruation (both before and after OS) is preferred by transmen but there are no data available to inform treatment protocols to minimise this."
BLEFCO	79	201	"GAHT" needs to be replaced by "GATH"	GAHT is the abbreviation of gender-affirming hormone treatment, and hence correct.
BLEFCO	80	225	The sentence "ovarian stimulation can impact negatively on gender dysphoria, and hence sensitivity and awareness and protocol adaptation can be considered." is unclear. Please reformulate.	We deleted the sentence, as a similar statement was included in the evidence section
D3. Oocyte cryopreservation				
BFS	82	32	previous cancer treatment: how long after completion of chemotherapy should ovrian stimulation be carried out? Discussion about monitoring return of menstruation/ Monitor AMH?	We have only briefly discussed FP after chemotherapy as an option (in part A, second phase of FP), as there is very little information to use as a base for relevant recommendations. We did, based on this comment, add a research recommendation on the topic

Fernando J. Prados-Mondéjar	82	19	It is written "Mangli" and should be: "Mangili"	This was corrected in the text,
Fernando J. Prados-Mondéjar	82	35	It is written: "it has shown" and should be: "it has been shown"	This was corrected in the text,
BLEFCO	82	9	Please add a full stop at the end of the sentence.	This was corrected in the text,
BLEFCO	82	19	"Mangli"may be replaced by "Mangili"	This was corrected in the text,
Carlos Calhaz-Jorge	83	91	The cited paper (Lekovich *et al.*, 2016) Lekovich J, Lobel ALS, Stewart JD, Pereira N, Kligman I, Rosenwaks Z. Female patients with lymphoma demonstrate diminished ovarian reserve even before initiation of chemotherapy when compared with healthy controls and patients with other malignancies. *Journal of assisted reproduction and genetics* 2016;33: 657-662. does not address results of transfer cycles.	We have corrected the reference to Alvarez et al 2016
Fernando J. Prados-Mondéjar	83	72	A space should be added after "cryopreservation"	This was corrected in the text,
Fernando J. Prados-Mondéjar	83	77	It should be: "differences such <u>as</u> lower"	This was corrected in the text,
Fernando J. Prados-Mondéjar	83	91	Should be: "and <u>a</u> cumulative PR per patient <u>of</u> 54.5%"	This was corrected in the text,
BLEFCO	83	53-55	"In women with breast cancer, carriers of a BRCA mutation have also presented with similar…" may be replaced by " In women with breast cancer, carriers of a BRCA mutation also presented similar…"	This was corrected in the text,
BFS	84	102	Suggest to include ovarian torsion in list of complications	In the literature review we did not find torsion as complication of these procedures for FP. In general ovarian torsion is a very rare complication
Fernando J. Prados-Mondéjar	85	152	"the woman <u>will</u> ~~is~~ not be able"	This was corrected in the text,
D4. Oocyte cryopreservation for age-related fertility loss				

Heidi Mertes	88	1	Title: Please reconsider title. In other contexts aging is not considered a non-medical reason either, e.g. we do not say that people who buy glasses because their eyesight is deteriorating with age buy them for non-medical reasons… Maybe best to maintain the terminology that the ESHRE Ethics taskforce used: "OC for age related fertility loss"	We have changed this and added a paragraph discussing terminology.
Heidi Mertes	88	3	Also elective egg freezing has been critizised as a term. Egg freezing is as elective for cancer patients as for patients facing age related fertility decline…	We have removed "elective" from the text
Heidi Mertes	88	39	I am a bit surprised that this argument for AGE banking is stressed in this document, as it is not the best one in the debate in my opinion. The reproductive lifespan is only marginally extended as most countries have a maximum age limit for the use of ARTs (usually mid-40s) and women bank in their late 30's. The few 'extra' years (which are not certain to start with given the limited success rates) therefore have a marginal effect on gender inequality + now it sounds too much as if women are certain to gain a couple of years this way, whereas it is oftentimes a long shot…	Assessing the text, we disagree that we stress this, but still, we have added limitations on the 'delay' later in the text
Shelley Grant	88	15 - D4	This section omits a potentially useful summary presentation, for clinicians, on the information opportunities occurring within typical care routines. Here, scientific estimates on FP risks to non-scientific could be presented to assist patient decisions. It would constitute a clinical tool for improving patient education in which information categories or topics are included in a schematic rendering of processes for the targeted FP populations in this guideline. Any graphic could include risks associated with key health outcomes with FP or overall (survival, recovery from benign diseases and the preservation of fertility capacity), and/or windows for care team members to address other decisions (e.g. costs, age limits to care, storage terms, etc.). A graphical display could summarize information opportunities across branches for each of the four distinct patient populations (page 6, lines 43-48). This suggestion is inspired by tools recently proposed in the "ESHRE Guidance on Recommending ART Treatments" published on the ESHRE website (on 23/04/2020) by the ESHRE COVID-19 Working Group. Model displays (information tools) in this document are the 1) "Summary Figure Patient Triage" (pg. 3) and 2) the "Summary Figure Treatment Cycle" (pg. 7). Note: these graphics effectively frame informational opportunities within the routine timing of needs for decisions and care intervention based on population-specific sets of risk. Placement of any graphic could be: • a set of population-specific displays, each placed at the introduction or conclusion of discussions on specific risks with one or two references to the primary concern involved in communicating or interpreting the risks of that group • as a comprehensive chart added among the existing graphics under the "List	We have assessed this comment, but decided not to make any adaptations to the text, or add any graphics to this section.

			of all recommendations" section (page 7, under "PART A: How should the care for women undergoing fertility preservation be organized?" • as an Appendix to the Guideline that is referenced in one or two sentences under a specific sub-section of FP population text, headed by a descriptive title for the population and the dominant associated risk(s) for that group.	
Carlos Calhaz-Jorge	88	26-30	Their content is totally repeated in lines 59-60.	We slightly rephrased and shortened the second time the RCOG document was mentioned, Thank you for alerting us.
Heidi Mertes	89	55	maybe clarify that 'medicalisation' as used here refers to a medical solution being offered for a societal problem, which may deviate attention from solving the root causes of delayed childbearing (several authors - including me - have argued that this objection is not strong enough in itself to argue against OC, but still, it is a prominent argument, especially in the feminist literature)	We added this point in the text
Heidi Mertes	89	56-58	I suggest rephrasing this sentence to: "However, both ESHRE and ASRM have concluded that oocyte cryopreservation for age related fertility decline does not produce harms that are not present in the context of OC for patients facing gonadotoxic treatments and therefore it is inconsistent to restrict its use to the latter group." The ESHRE and ASRM statements certainly did not conclude that there are no potential harms. Quite the contrary, they set out requirements that should be fulfilled to prevent harm (mostly aimed at informed decision making). The statements only rejected the restriction to use in oncofertility at the expense of age-related applications, which I think is the point that was meant here. gonadotoxic treatments and therefore it is inconsistent to restrict its use to the latter group." The ESHRE and ASRM statements certainly did not conclude that there are no potential harms. Quite the contrary, they set out requirements that should be fulfilled to prevent harm (mostly aimed at informed decision making). The statements only rejected the restriction to use in oncofertility at the expense of age-related applications, which I think is the point that was meant here.	It is not stated in the text that the ASRM or ESHRE said there were no harms. We have added in the point about not restricting its use to 'medical' uses, and rephrased the text a bit.
Heidi Mertes	89	80-81	Please be careful about framing AGE banking as a way to 'delay childbirth', as this is not consistent with reality (at this point in time at least) and not an evolution that is desirable. Oocyte cryopreservation is seldom a way for women who could have their children today to 'delay' childbearing to a later point in time. The main reason for AGE-banking is lack of a partner (and thus inability to reproduce 'early') combined with the end of the reproductive lifespan, so delay of childbirth is not a result of choosing AGE banking, rather, these are women who already 'delayed' and who either (1) will not have any children because their ovarian reserve is depleted by the time they find the right partner, (2) have children 'later' with their aged oocytes (with a higher risk of congenital abnormalities and pregnancy complications), (3) have children 'later' with donor oocytes or (4) have children 'later' with their previously cryopreserved oocytes (with a risk of	We addressed this comment in the text

			congenital abnormalities and pregnancy complications in between the option of donor oocytes and own aged oocytes). In conclusion, OC may lead to a couple of mothers who have a child at 45 instead of none and their extra pregnancy complications will be limited to uterine factors and their general physical health, not to oocyte factors, which also makes a big difference.	
Heidi Mertes	89	99	'Ethics': all of the above point are also 'ethics' :-) Maybe call this "undue pressure" or something similar.	We have changed the heading to "Company sponsored oocyte cryopreservation"
Carlos Calhaz-Jorge	89	70-71	"oocytes) (Cobo et al., 2018). However, a maximum CLBR of 50% was achieved by those who froze when they were over 35" is again misleading. Please consider "a maximum CLBR of 50% was achieved by those who froze when they were over 35, after using 20 or more thawed oocytes".	The sentence was adapted as suggested by the reviewer
Heidi Mertes	89	81	In addition to the previous comment, why is the reference used here looking at the general population (in which age of the woman is the same as age of the oocyte)? I know that there is conflicting data on the extent to which pregnancy complications in 'older' women are due to the age of the oocyte or to other factors, and I know that donor cycles are not a good point of reference either as they present a risk factor it itself, but given that this group will have the benefit of 'younger' eggs, and the benefit of own eggs does mean that they are likely to suffer less complications than other women in the same age group in the general population.	We have checked the reference and the study and consider it appropriate to use the reference to support that pregnancy carries an increased risk in older women.
Carlos Calhaz-Jorge	89	69	"approaching 95% provided sufficient oocytes were obtained" is misleading. Ana Cobo's paper refers to "utilised oocytes", not cryopreserved. Unfortunately survival rate after thawing is not 100%. Please consider "approaching 95% in cases with 24 or more utilised thawed oocytes" It is said that elective cryopreservation of oocytes may have a CLBR "approaching 95%" Please check. Maybe it refers to oocytes survival rate. For sure not CLBR	The paper states : The plateau in the subgroup of young women (≤35 year) was reached with 24 oocytes, and also with a remarkably high success rate (94.4% [95%CI = 84.3–100.4] CLBR). We have adapted the sentence as suggested, but we have not adapted the CLBR of 95%.
Carlos Calhaz-Jorge	89	83-85	Missing word(s)? Sentence seems incomplete.	This was corrected in the text,
D5. Embryo cryopreservation				
Carlos Calhaz-Jorge	93	82	" 20% at cleavage stage " should be 38%	We have checked the paper and corrected this error in the guidelines
Fernando J. Prados-Mondéjar	93	49	"than slow-~~freeze~~ freezing"	This was corrected in the text,

D6. Ovarian tissue cryopreservation				
BLEFCO	97	63-65	A recent paper (Pretalli JB, Frontczak Franck S, Pazart L, Roux C, Amiot C; DATOR Group. Development of Ovarian Tissue Autograft to Restore Ovarian Function: Protocol for a French Multicenter Cohort Study. JMIR Res Protoc. 2019 Sep 30;8(9) reports the outcome of 14births after grafting of OTC. This paper may be mentioned as reference to update the number of livebirths obtained in Europe after OTC.	We have added the reference and updated the numbers.
Carlos Calhaz-Jorge	100	186	There It is necessary to have appropriate equipment - Please remove "There"	This was corrected in the text,
Carlos Calhaz-Jorge	101	217	Recommendation: "Young patients who have …" Can the authors please clarify how should "young" be read? Less than 35? 38?	We agree that "young" is confusing and as we defined the conditions in the text, it was decided to remove it from the recommendation,
BLEFCO	102	276 - 279	The established alternatives (egg donation or others) may be mentioned. Finally, is it better to recommend only autotransplantation?	We have clarified the alternatives (oocyte donation)
Carlos Calhaz-Jorge	102	280	Recommendation: **"OTT can be considered in patients with POI-associated genetic and "**Maybe better "OTC/OTT can be considered…"	This was adapted as suggested
BLEFCO	103	327	The publication of Sanfilippo et al., 2015 (Sanfilippo S, Canis M, Smitz J, Sion B, Darcha C, Janny L, Brugnon F. Vitrification of human ovarian tissue : a practical and relevant alternative to slow freezing. Reprod Biol Endocrinol 13: 67-74) .showed no difference between not only follicles density but also DNA fragmentation of follicles and stroma cells between slow freezing and vitrification. This publication may be cited.	We decided not to add this publication, as the data were included in the meta-analysis of Shi 2017,
BLEFCO	104	352	The french cohort study reported in the publication of Pretalli *et al.*, 2019 may be mentioned.	We added the reference to the guideline
Gareth Greggains	104	348	It would be useful to have recommendations also on post OTT management eg. whether it is better to go directly to IVF or try in the first instance to conceive spontaneously for 4 months after OTC.	Post OTT management was not within the scope of this guideline. However, we specify that natural conception is an important benefit of OTC which implies that it is not recommended to proceed straight to IVF
BLEFCO	104	347	This is a general remark: we think it is important to notify about the safety of cryostorage for example: "The cryostorage of gametes, ovarian tissue or embryos must be ensured with a 24-hour monitoring alarm".	We agree but has already been mentioned in a general statement reading "high quality control assurance including specific laboratory training distinct from that in 'standard' ART" for OCT

Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	106	433 - 438	Page 106 Line 433-438-and page 108 line 503-. (Table 9) In the draft there is the text "Haematological malignancies: The conclusion on the draft is that OTT could be offered in leukaemia patients if OTC has been performed at the time of bone marrow remission, after investigations." There is a reference to an article by Kirsi Jahnukainen -13. She has reviewed on this conclusion, and she states: "In conclusion, our data indicate that postponing the fertility preservation measures to the time of leukemia remission with no bone marrow MRD results in less or no leukemic contamination in the ovarian material. However, the correlation between the bone marrow and ovarian MRD is not complete, and significant leukemic contamination may be present in ovarian tissue during marrow remission." Investigating other tissue pieces would not be conclusive of the safety of the ones that would be transplanted, and transplant should not be recommended, even with caution.	We have adapted the paragraph and the table accordingly.
E.E.L.O.Lashley	11	37	As the effect of OTC has never been compared to a non intervention group (as the PICO states) we suggest that this line is changed into; OTC is *probably* an effective method	In reply to this comment, we have removed the sentence from the recommendation, leaving only "It is recommended to offer OTC in patients undergoing moderate/high risk gonadotoxic treatment where oocyte/embryo cryopreservation is not feasible, or at patient preference."
E.E.L.O.Lashley	11	38	We would suggest not to use a threshold, but a percentile (p<5) specified per age. It oocyte preservation is not an option, OTC should also be mentioned in women aged > 36years. If oocyte preservation is an option, this is superior to OTC. So why include an age limit?	We have assessed this comment and decided to keep a threshold of 0,5ng/ml consistent with the Bologna criteria, as this is more straightforward, We decided to keep the age limit, but reformulated the sentence.
E.E.L.O.Lashley	12	55	Remove probably. These data are very much recommended!	As suggested, we removed the word "probably" from the recommendation
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	12	51	The patient should be informed on the risks.	We have added "and patients should be informed about this risk." to the recommendation
Aboubakr Mohamed Elnashar	13	38	Low ovarian reserve should be less than 0.5 ng/ml not less than 0.4ng/ml	The threshold in the recommendation was based on the results of the study from Paradisi 2016, but the GDG agrees to be consistent and use the threshold used in the Bologna criteria, ie 0.5 ng/ml. in the recommendation
Carlos Calhaz-Jorge	106	459 (an	Suggest central nervous system instead of central nerve system	This was corrected in the text,

		d Tab leg)		
BFS	107	496	Be aware that recommendations are often read in isolation, "Endometrial cancer is not a contraindication for… pregnancy" is suprising for a condition where hysterectomy is the primary treatment	We have modified the recommendation.
Carlos Calhaz-Jorge	109	541	Recommendation: **"Long-term risks in human are considered to be low but a long-term follow-up of patients after OTT is probably recommended"** The word "probably" sounds strange in this context (plus considering that it is a GPP). Can it be deleted?	As suggested, we removed the word "probably" from the recommendation
BFS	110	542	Would like to see discussion reflected in recommendation that egg freezing is a more sensible option for BRCA patients as avoids the risk of regrafting tissue with malignant potential	The recommendation was adapted accordingly
Margarita Chrysanthou Piterou	110	551-553	Please confirm if this recommendation exists also in healthy carriers of germline BRCA mutations who have a great risk for ovarian cancer and often choose to perform bilateral oophorectomy	We have revised the justification accordingly.
Carlos Calhaz-Jorge	110	551	*Although there is no evidence for malignant transformation of or ovarian cancer originating* Please remove "or"	This was corrected in the text, we removed "of"
D7 In vitro maturation (IVM)				
BLEFCO	114	31	We propose to add the first publication about IVM in PCOS patients (Trounson AO, Wood C, Kausche A. In-vitro maturation and the fertilization and developmental competence of oocytes recovered from untreated polycystic ovarian patients, Fertil Steril 1994, 62 (353-362).	We only briefly mention PCOS in the introduction of the IVM chapter, but as the goal of IVM in PCOS patients is not generally fertility preservation, we did not include further studies on the topic in the IVM chapter
Michel De Vos - Ingrid Segers	116	116	"Since the first report of two cases (Isachenko et al., 2004), …" -> The first description of the technique and first IVM of ovarian tissue oocytes (OTO) was published by Revel et al.: Revel A, Koler M, Simon A, Lewin A, Laufer N, Safran A. Oocyte collection during cryopreservation of the ovarian cortex. Fertil Steril 2003;79: 1237-1239.	We have adapted the sentence based on this comment and added the reference
Michel De Vos - Ingrid Segers	116	126	In the study of Hourvitz et al., which is referred to in this statement, 142 patients underwent ovarian tissue cryopreservation only (OTC), 56 underwent OTC plus oocyte retrieval from ovarian tissue (OTO-IVM), nine underwent oocyte aspiration and in-vitro maturation and 48 underwent all three procedures. In this study, OTO-IVM was used as an appended technique in addition to ovarian tissue biopsies. Since ovarian biopsies will yield a lesser amount of medulla compared to whole ovaries, the number of OTO-IVM oocytes will be relatively limited when biospies are performed as compared to oophorectomy. Therefore,	We added a sentence on the Hourvitz paper. As the paper of Segers 2020 was not published at the time of finalisation of the guideline, it could not be added in the clinical evidence, but we added a footnote mentioning the paper.

			this paper may not reflect the true potential of OTO-IVM. Our group has a recent paper, which was accepted for publication in Human Reproduction, describing vitrification of 6.7 +/- 6.3 oocytes in 64 patients who had unilateral oophorectomy for OTC (Segers et al., LIVE BIRTHS FOLLOWING FERTILITY PRESERVATION USING IN VITRO MATURATION OF OVARIAN TISSUE OOCYTES, accepted for publication in Hum Reprod 2020).	
Michel De Vos - Ingrid Segers	116	130	" after 48h culture" -> should be " after 24h-48h culture"	This was corrected in the paper
Dmitry Nikiforov	116	120	In the draft of a guideline the in vitro maturation of ex vivo collected human oocytes is being discussed and as an academic and clinical organization, practicing in vitro maturation, we would like to highlight that a recovery range of human oocytes in mentioned model is much higher than 58 oocytes, as it states now in the draft guideline. A recent publication demonstrated that an average of 36 immature oocytes can be collected and as many as 90 immature human oocytes can be recovered from one ovary. We suggest it is an important number, representing a substantial prospective for augmenting chances of conception in patients undergoing ovarian cortex freezing in combination with in vitro maturation of oocytes from surplus tissue. Reference: Nikiforov D , Junping C, Cadenas J, Shukla V, Blanshard R , Pors SE , Kristensen SG , Macklon KT, Colmorn L, Ernst E , Bay-Bjørn AM , Ghezelayagh Z, Wakimoto Y, Grøndahl ML, Hoffmann E , Andersen CY. Improving the Maturation Rate of Human Oocytes Collected Ex Vivo During the Cryopreservation of Ovarian Tissue. J Assist Reprod Genet . 2020 Apr;37(4):891-904. doi: 10.1007/s10815-020-01724-7.	Thank you for this comment. As the paper was published after the inclusion deadline and it did not significantly impact our conclusion, we decided not to add the reference.
Michel De Vos - Ingrid Segers	117	153	Further to the data reported in Segers et al., 2015, updated data can be found in our new paper (Segers et al., accepted for publication in Hum Reprod 2020). In that paper, one further healthy live birth following OTO-IVM derived embryo vitrification is reported (which gives a total of four live births after OTO-IVM derived embryo vitrification): a breast cancer patient who was 36-year old when she had OTC + OTO-IVM (Segers et al. 2020). Moreover, one case of a healthy live born is reported in that same paper, following transfer of an embryo originating from vitrified/warmed OTO-IVM oocytes in a 23-year old Hodgkin Lymphoma patient (Segers et al. accepted for publication in Hum Reprod 2020).	As the paper of Segers 2020 was not published at the time of finalisation of the guideline, it could not be added in the clinical evidence; we have added a footnote mentioning the paper.
D8. GnRH agonist				
M.H.Mochtar	121	71	The committee states that GnRH should be offered, however limited evidence for ovarian reserve and further pregnancies, while the recommendations is labelled strong evidence? What is in this context then the definition of ovarian protection?	GnRHa should be offered for preservation of ovarian function, for which there is strong evidence of benefit. For fertility outcomes, the evidence is less convincing. The difference between ovarian function protection (prevention of POI) and fertility

				outcomes is explained in the introduction of the chapter.
Hanna Savolainen-Peltonen, Eini Nikander, Varpu Ranta	13	62	#62, page 13: Although there is no clear evidence for ovarian function protection in other malignancies than possibly breast cancer, there may be other medical benefits of using them during chemotherapy (such as heavy menstrual bleeding). Could that be raised up in the recommendation, not only in the text?	Reading this and other comments, we have slightly rephrased the recommendation to make it less stringent. It now reads "In malignancies other than breast cancer, GnRH agonists should not be routinely offered as an option for ovarian function protection and fertility preservation without discussion of the uncertainty about its benefit". It was decided not to further elaborate on other benefits in the recommendation.
Dr. Bettina Böttcher/ Prof. Dr. Bettina Toth	122		We were surprised about the strong recommendation not to apply GnRH to non breast cancer patients based on the data of 108 patients. Should the recommendation not be differentiated with regard to the applied chemotherapy regimen, Regimen such as ABVD or BEACOPP esc? Otherwise, it could be stated that the patient should be informed about limited data and benefit in other than breast cancer patients?	Reading this and other comments, we have slightly rephrased the recommendation to make it less stringent. It now reads "In malignancies other than breast cancer, GnRH agonists should not be routinely offered as an option for ovarian function protection and fertility preservation without discussion of the uncertainty about its benefit". It was decided not to further elaborate on other benefits in the recommendation.
BFS	122	110	Significantly higher AMH were seen in women after treatment for Hodgkins lymphoma at 1 year but not at later follow up, could GnRH agonist be t used for those patients medically unfit for FP prior to chemotherapy so that they get another window of opportunity later?	We agree with this remark; this was already addressed in the guideline in the good practice point "GnRH agonists should not be considered an equivalent or alternative option for fertility preservation but can be offered after cryopreservation techniques or when they are not possible."
GGOLFB	122	113	typing error at the § beginning: ". An"	This was corrected in the text.

BFS	123	125	The strong negative recommendation "in malignancies other than breast cancer GnHR agonists should not be offered" is not justified. The statement implies that there is good evidence against their use across the spectrum. However, there is a complete absence of evidence in most other malignancies.	While we recognise that it would be unreasonable to require evidence for all possible cancers, we do not consider that evidence from breast cancer can be reliably extrapolated to other conditions with very different patient age ranges and chemotherapy regimens. The limited available evidence in lymphoma does not suggest a possible protective effect of GnRH agonists in preserving ovarian function. However, on considering this and other comments, we have slightly rephrased the recommendation to make it less stringent. It now reads "In malignancies other than breast cancer, GnRH agonists should not be routinely offered as an option for ovarian function protection and fertility preservation without discussion of the uncertainty about its benefit".
D9. Ovarian transposition				
GGOLFB	128	99	"…metastasis were not find" but in line 96 it is mentioned "ovarian metastasis were also reported" and the reference (Gubbala 2014) is the same.	We slightly rephrased the first sentence, explaining that the data were collected and assessed in the meta-analysis, but there were no reports of ovarian metastasis in the included studies.
BFS	128	102	Can there be a discussion about reversal of ovarian transposition after remission? Pros and cons and recommendations	We did not find any reliable information on reversal of ovarian transposition in the literature overview, and hence decided not to formulate recommendations on the topic.
Carlos Calhaz-Jorge	131	49-50	"(see section E1. Patient assessment prior to use of stored material)". It looks odd because we are in section E1.	This was corrected to E2 in the text,
E1. Patient assessment prior to use of stored material + E2. Obstetric outcomes				
Working Group for Reproductive Endocrinology of the Finnish Society of Obstetrics and Gynaecology	14	67	Assessment to rule out secondary malignancies before pregnancy should be mentioned.	We have added this sentence in the justification and in the figure.
BFS	15, 146	77, 278	This is an over-arching recommendation and should come first in this section	This recommendation summarises the different effects on the different cancers, and we consider its position appropriate and consistent with the other

				chapters, with the recommendations following the description of the topic,
BFS	130 - 148	n/a	We were very glad to see a section on later care – too often overlooked. Also to see information on future care and issues relating to future pregnancy included in pre-FP discussion	Thank you!
M.H.Mochtar	132	91	Welfare of het child should always be considered not only in transgender men, but also in women with gonadotoxic reason for FP or for social reasons.	We had already included the sentence "Local guidelines for treatment, taking into account the welfare of the child, should be followed" for other patient groups, and we have now also added it to checklist 1,
GGOLFB	137	28	It is mentioned that, in the publication of van der Kooi 2019, "incidence of congenital abnormalities was significantly higher" but in Table 10 p138 it is "no difference"	The table includes the observational study from van der Kooi 2018, which showed no difference. In the meta-analysis by the same author (2019), a RR of 1.10 was shown, but the paper stats "The risk of congenital abnormalities also appears increased (RR 1.10; 95% CI 1.02e1.20), but this is likely to be an artefact of analysis.' We adapted the guideline adding this statement from the review,
Carlos Calhaz-Jorge	137	12	A typo in (See Table 10)	This was corrected in the text,
GGOLFB	137	12	Typing error "tbale 10"	This was corrected in the text,
E.E.L.O.Lashley	14 and 137	69 and 30	Change: "anticancer" into gonadotoxic	We have adapted "anticancer" to "gonadotoxic" throughout the guideline
Carlos Calhaz-Jorge	139	48-49	"… became pregnant 50 times (range 1-6 times), resulting in 43 (86%) live births, 7 (14%) miscarriages, and 1 still birth (at 28 weeks)." The total – 43+7+1 – is 51. I suggest to replicate the sentence of the cited paper "7 (14%) miscarriages, including 1 still birth (at 28 weeks)".	This was corrected in the text,
Carlos Calhaz-Jorge	140	87	It would be better to explain the meaning of "TBI"	Abbreviation was spelled out and added to the abbreviations list
Carlos Calhaz-Jorge	143	211	The rate of recurrence in this series it was 5.1% in the fertility Suggest to remove "it"	This was corrected in the text,
Annexes				
Working Group for Reproductive	161	17	PICO is missing from the Abbreviations.	PICO was added to the abbreviations

Endocrinology of the Finnish Society of Obstetrics and Gynaecology				
Margarita Chrysanthou Piterou	162	17	There is no definition for GPP. Please add.	This was corrected in the text,
E.E.L.O.Lashley	162	31-32	Change: “anticancer” into gonadotoxic Remove cancer before patients	We have adapted "anticancer" to "gonadotoxic" throughout the guideline