The age, too old, the eggs too few
Clinical Perspective

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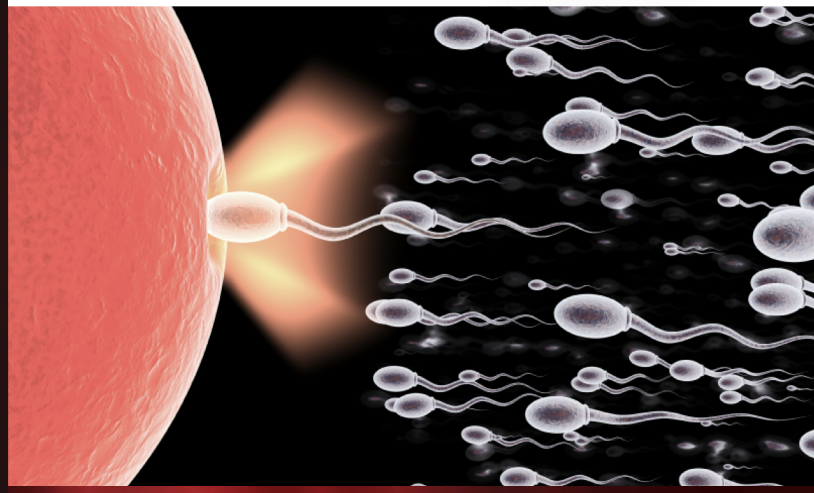


The age, too old…

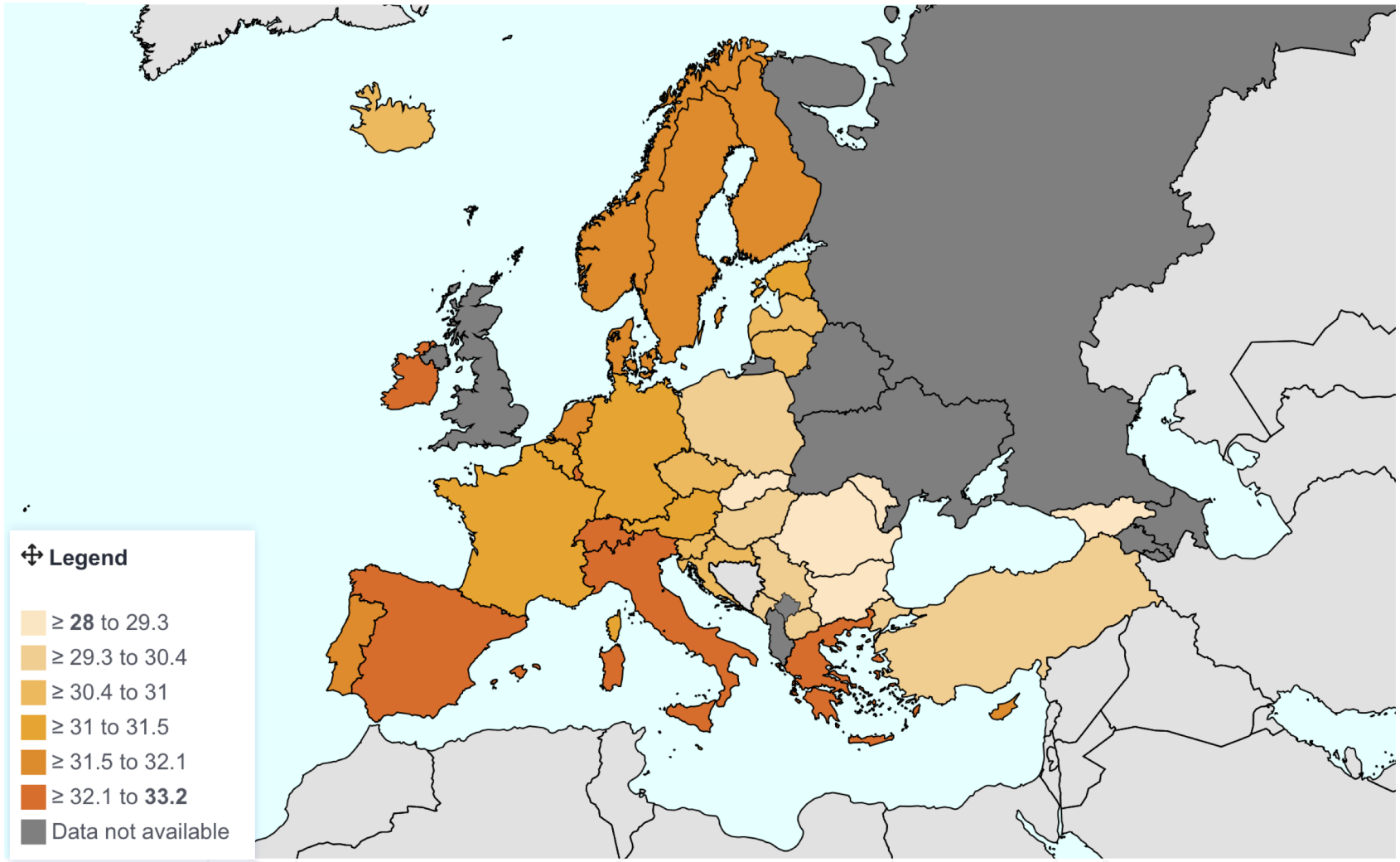
Motherhood

- https://drritabakshi.in/advanced-maternal-age-pregnancy-over-35/

The age, too old…

Motherhood

Mean age of women at childbirth (2023): 31.6



- https://ec.europa.eu/eurostat/databrowser/view/tps00017/default/map?lang=en

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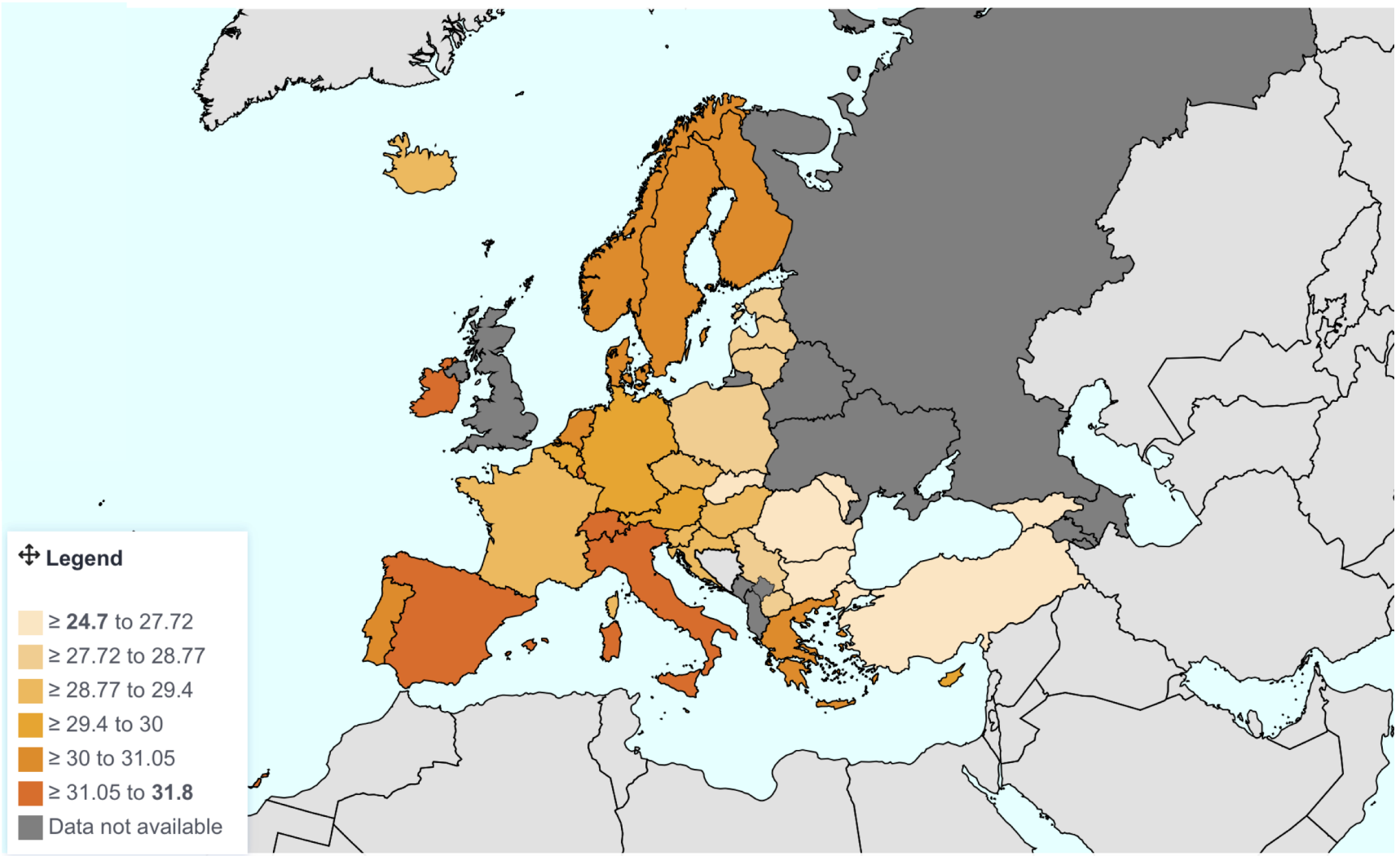
Motherhood

Mean age of women at birth of first child (2023): 30.2



- https://ec.europa.eu/eurostat/databrowser/view/tps00017/default/map?lang=en

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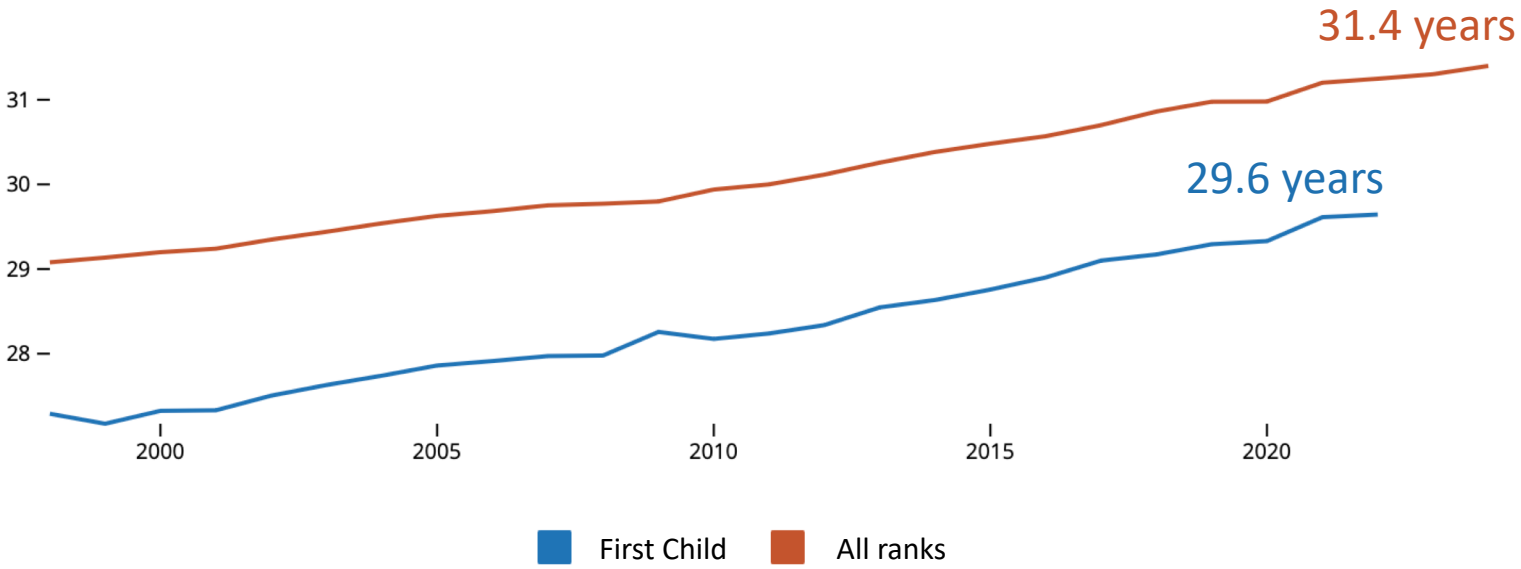
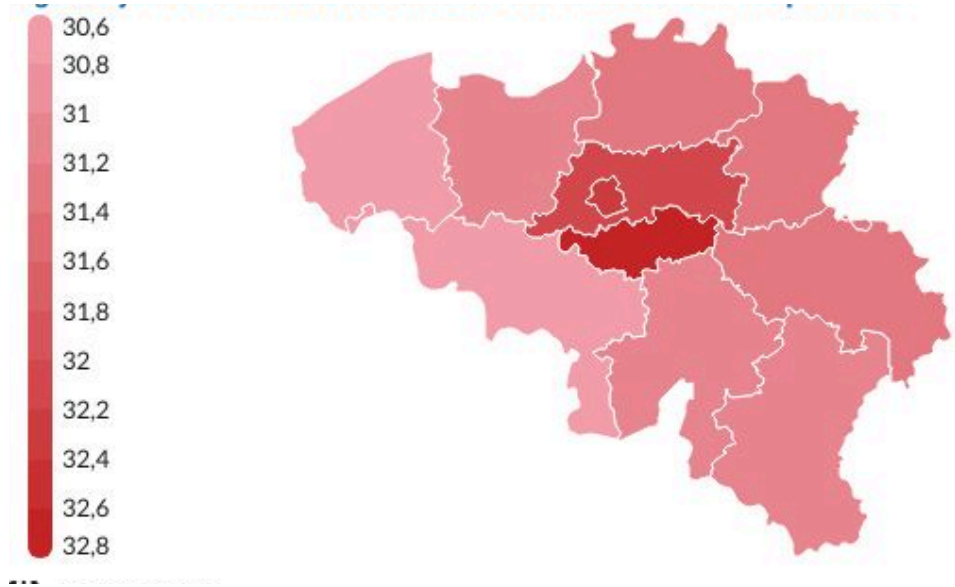
Motherhood

Mean age of women at childbirth and at birth of first child (2024)





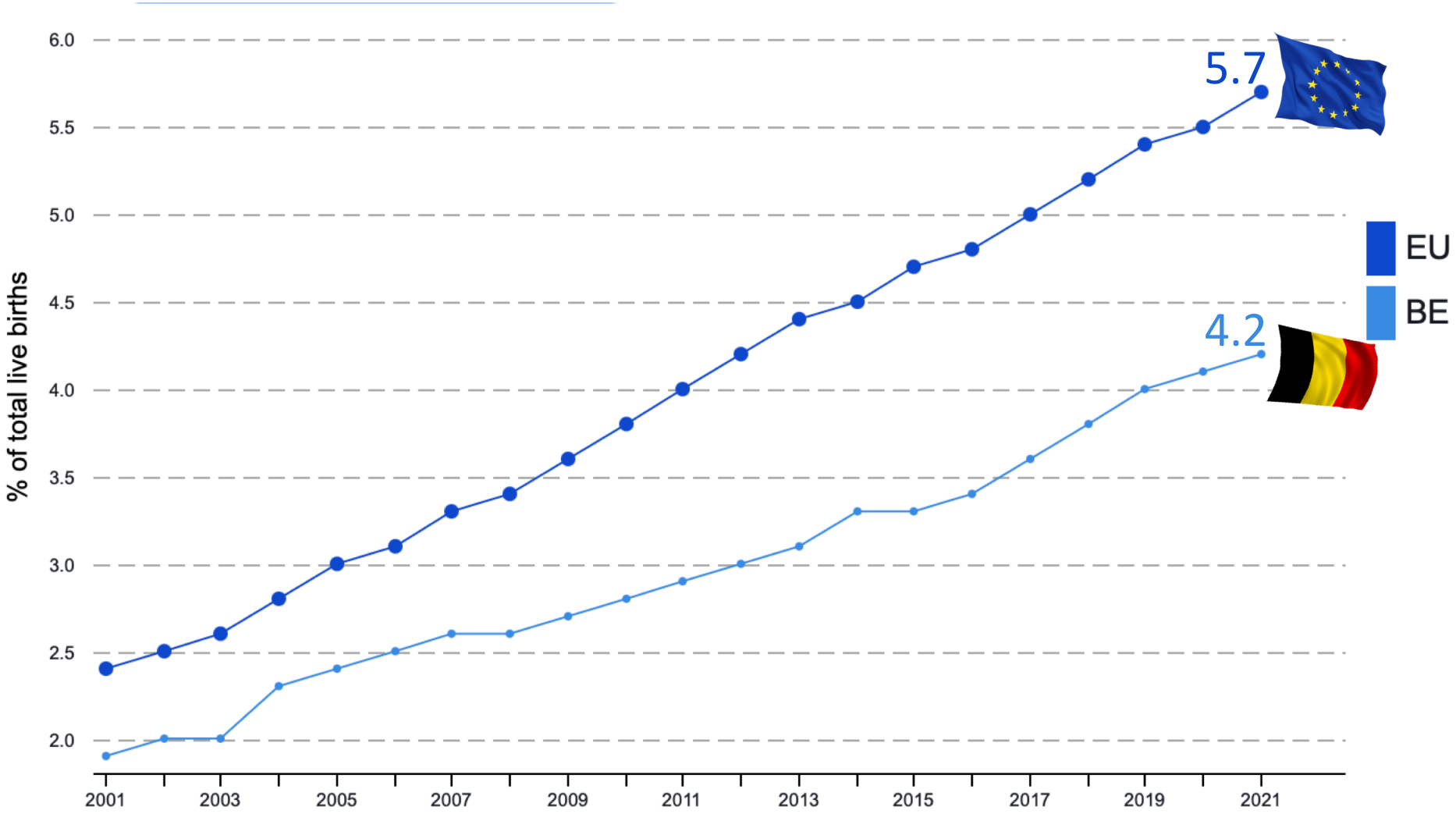
Mean age of fathers or co-parents is 34.3 years

- https://statbel.fgov.be/fr/themes/population/naissances-et-fecondite#figures

The age, too old…

Motherhood

Live births from mothers aged 40 and over
(as % of the total live births)



- https://ec.europa.eu/eurostat/web/interactive-publications/demography-2023#ageing-population

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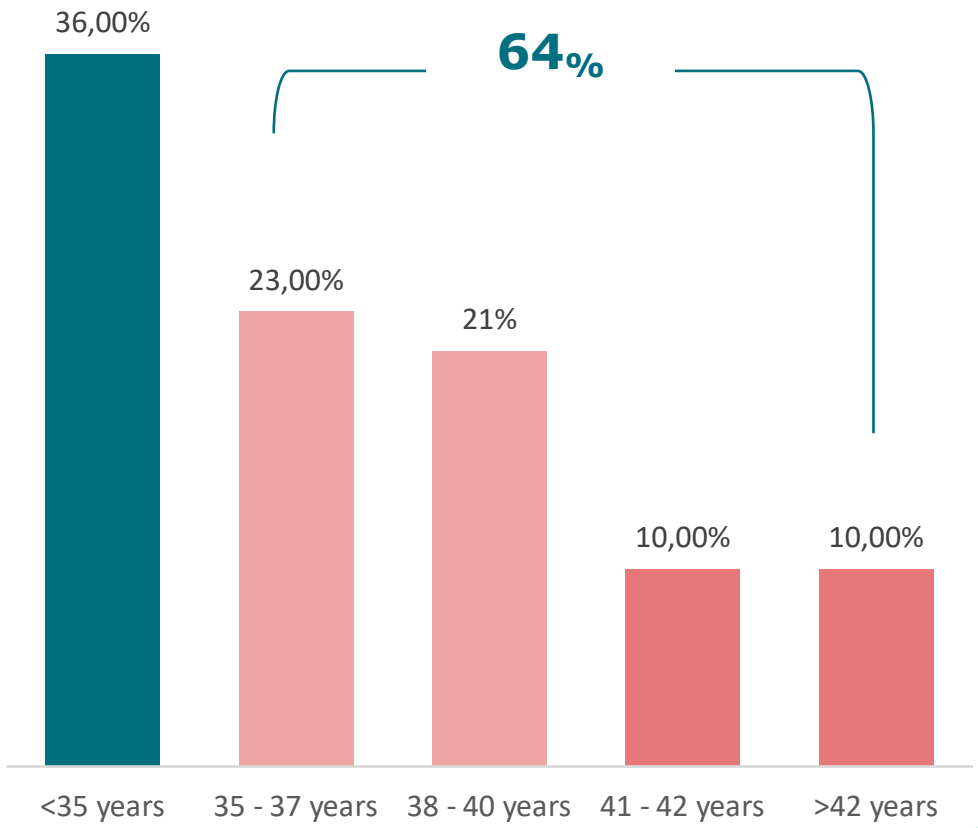
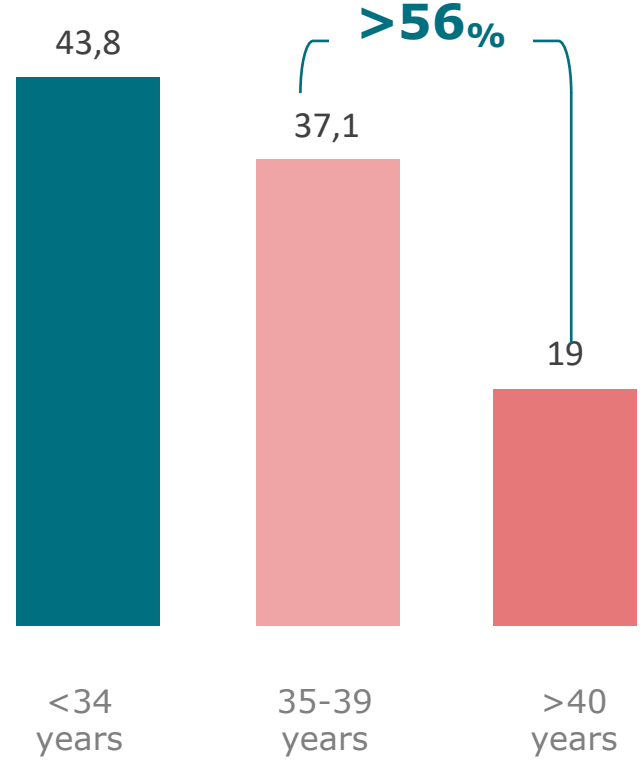
Fertility Treatments

CDC data for ART (2022)
64% of cycles are
≥ 35 years old



European IVF Monitoring Consortium (EIM) for ESHRE (2019)
56.1% of oocyte pick up are
≥ 35 years old



- https://www.cdc.gov/art/php/national-summary/index.html
- European IVF Monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE); Smeenk J, Wyns C, De Geyter C, Kupka M, Bergh C, Cuevas Saiz I, De Neubourg D, Rezabek K, Tandler-Schneider A, Rugescu I, Goossens V. ART in Europe, 2019: results generated from European registries by ESHRE†. Hum Reprod. 2023 Dec 4;38(12):2321-2338. doi: 10.1093/humrep/dead197

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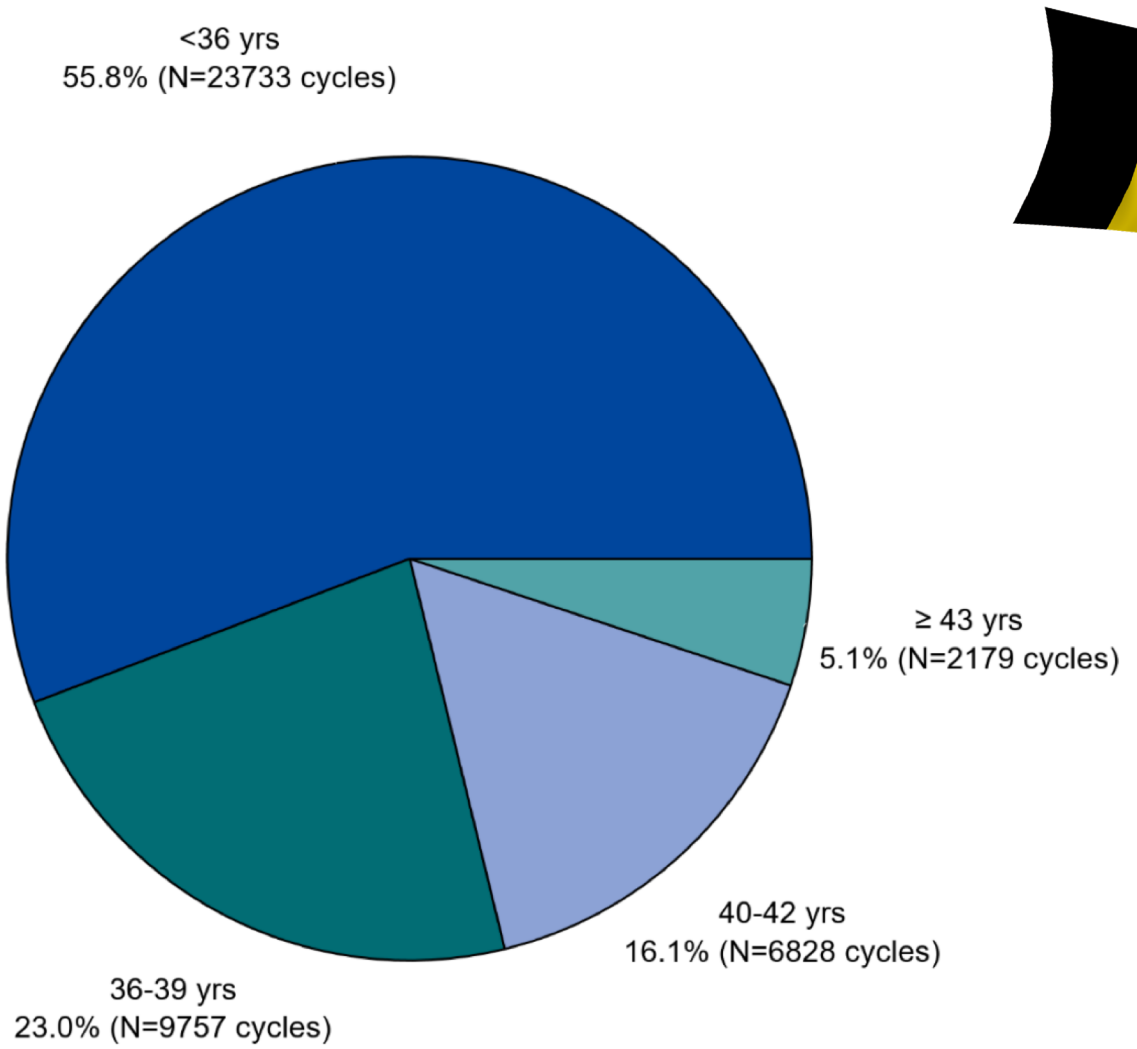
ART use by age group

BELRAP (2021)
44.2% of ART cycles are
≥ 36 years old



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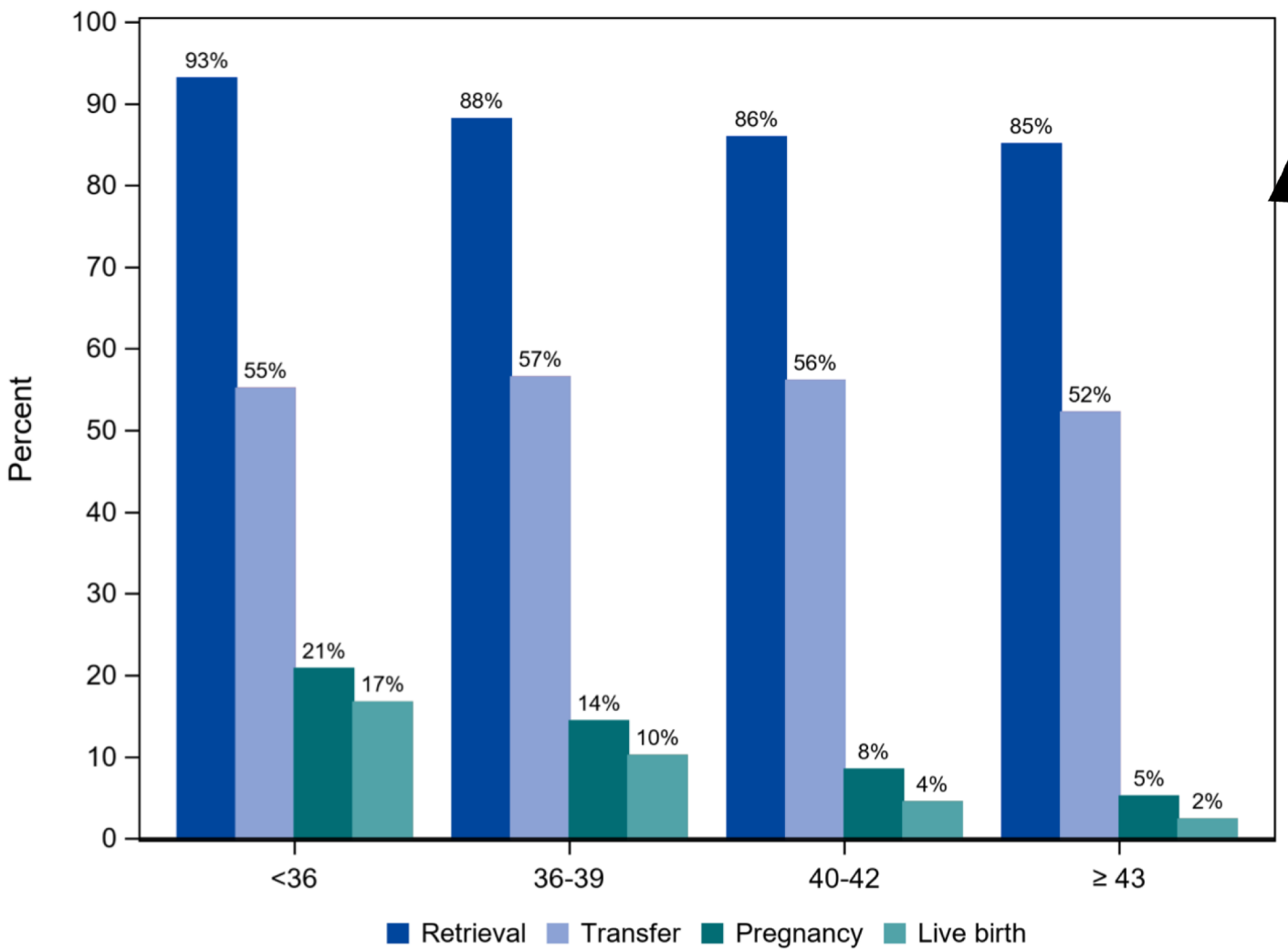
Fertility Treatments

Outcomes of ART cycles using fresh nondonor eggs or embryos, by stage and age group



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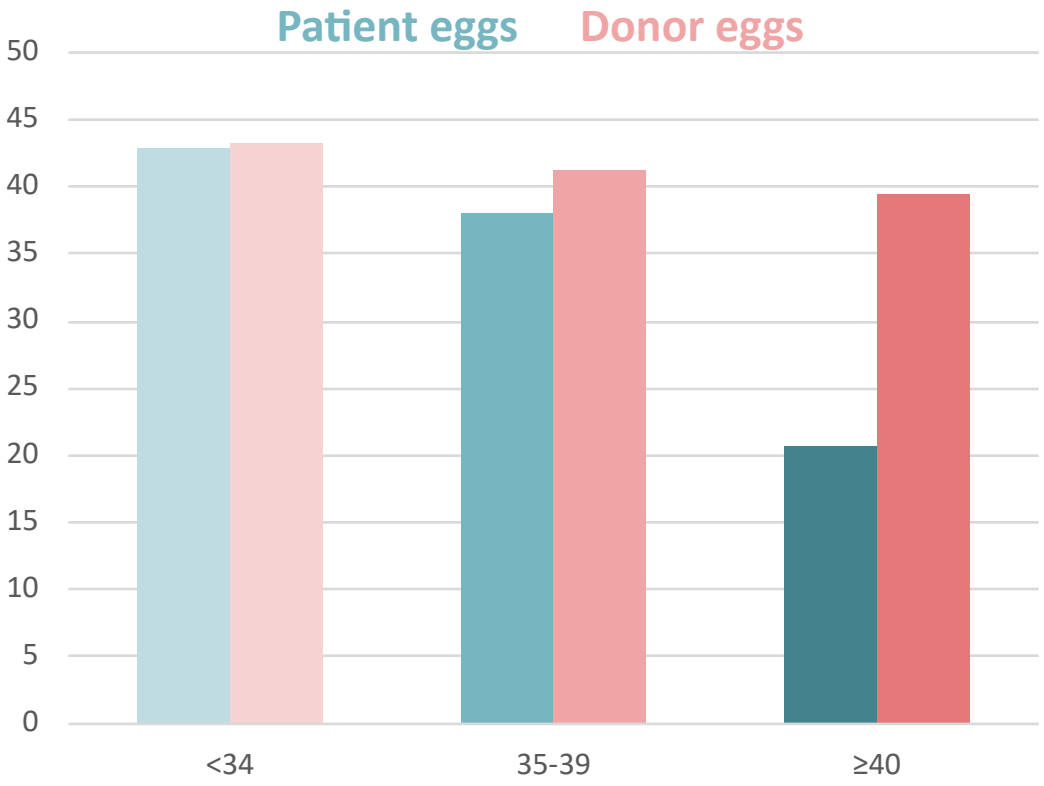
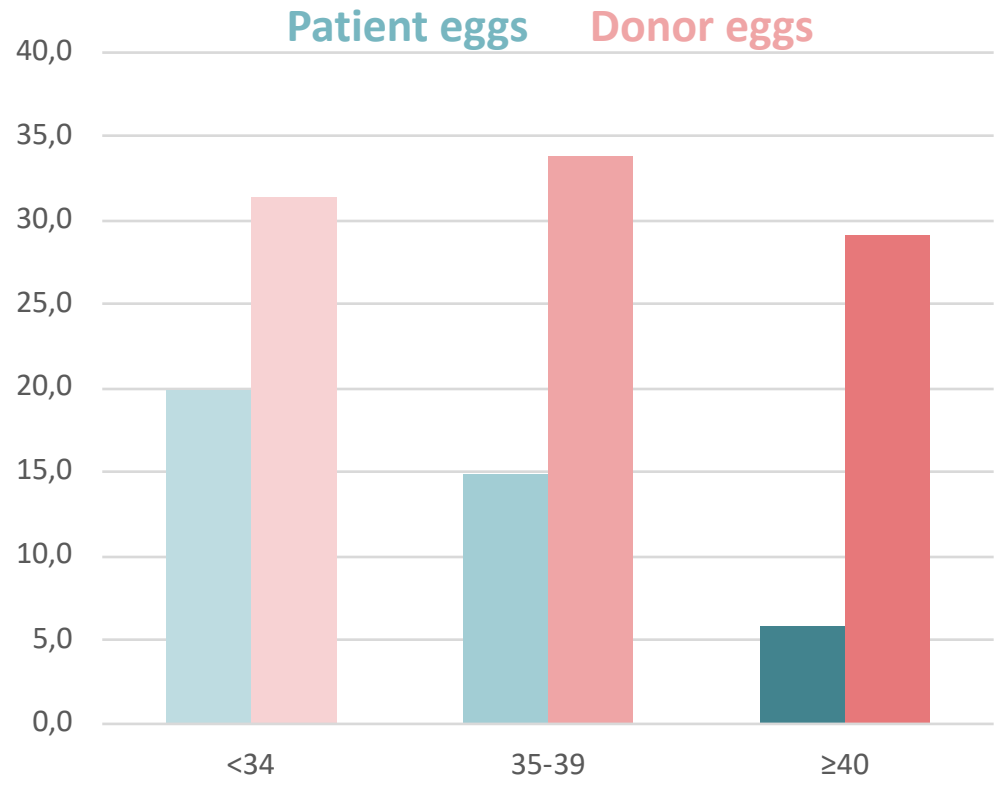
Fertility Treatments

US: Percentage of Embryo Transfers That Resulted in Live-Birth Delivery (2022)



UE: Percentage of IVF/ICSI That Resulted in Live-Birth Delivery (2019)



- https://www.cdc.gov/art/php/national-summary/index.html
- European IVF Monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE); Smeenk J, Wyns C, De Geyter C, Kupka M, Bergh C, Cuevas Saiz I, De Neubourg D, Rezabek K, Tandler-Schneider A, Rugescu I, Goossens V. ART in Europe, 2019: results generated from European registries by ESHRE†. Hum Reprod. 2023 Dec 4;38(12):2321-2338. doi: 10.1093/humrep/dead197

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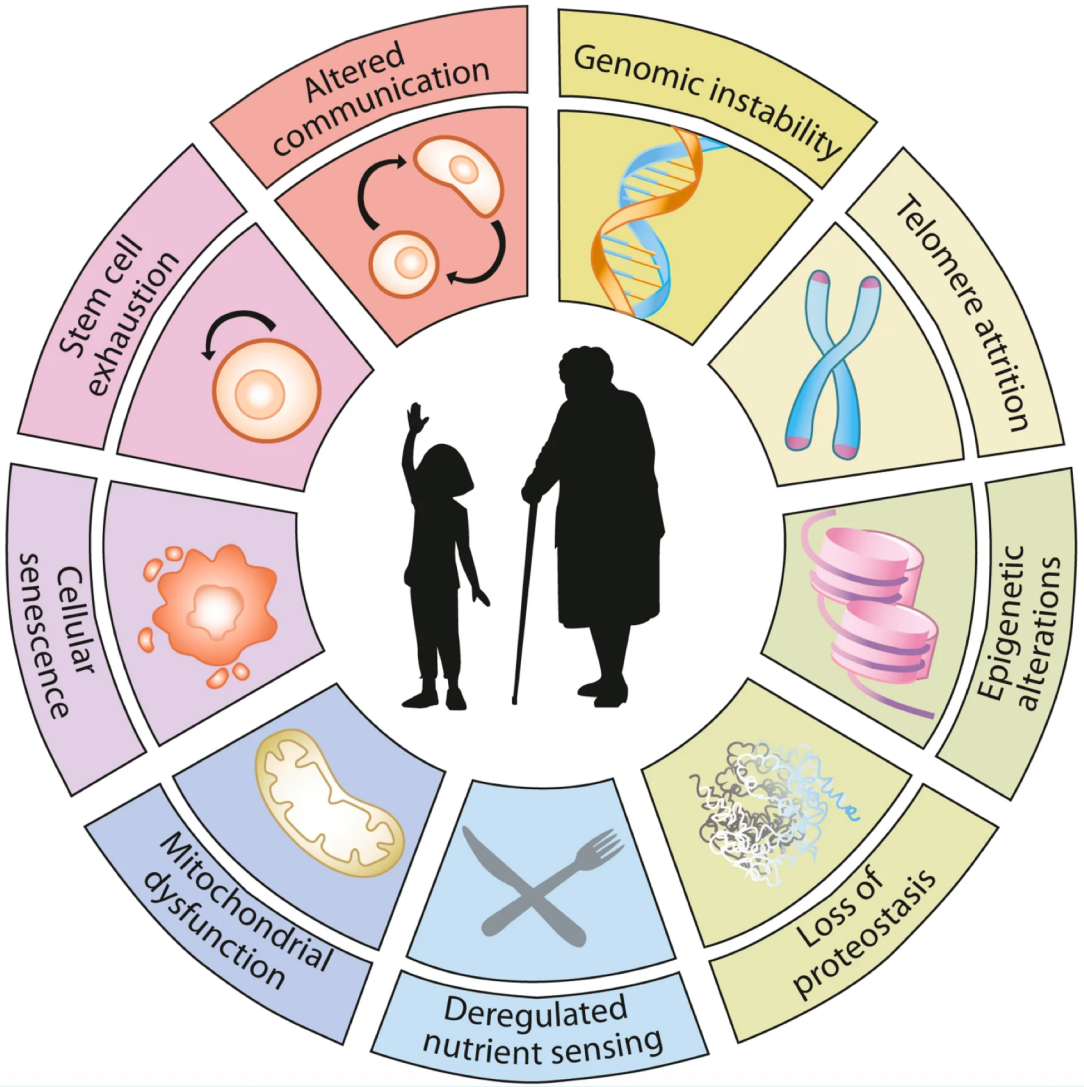
Hallmarks of aging



- Yen & Jaffe's Reproductive Endocrinology, Ninth Edition - Modified López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. Cell. 2013;153(6):1194–1217

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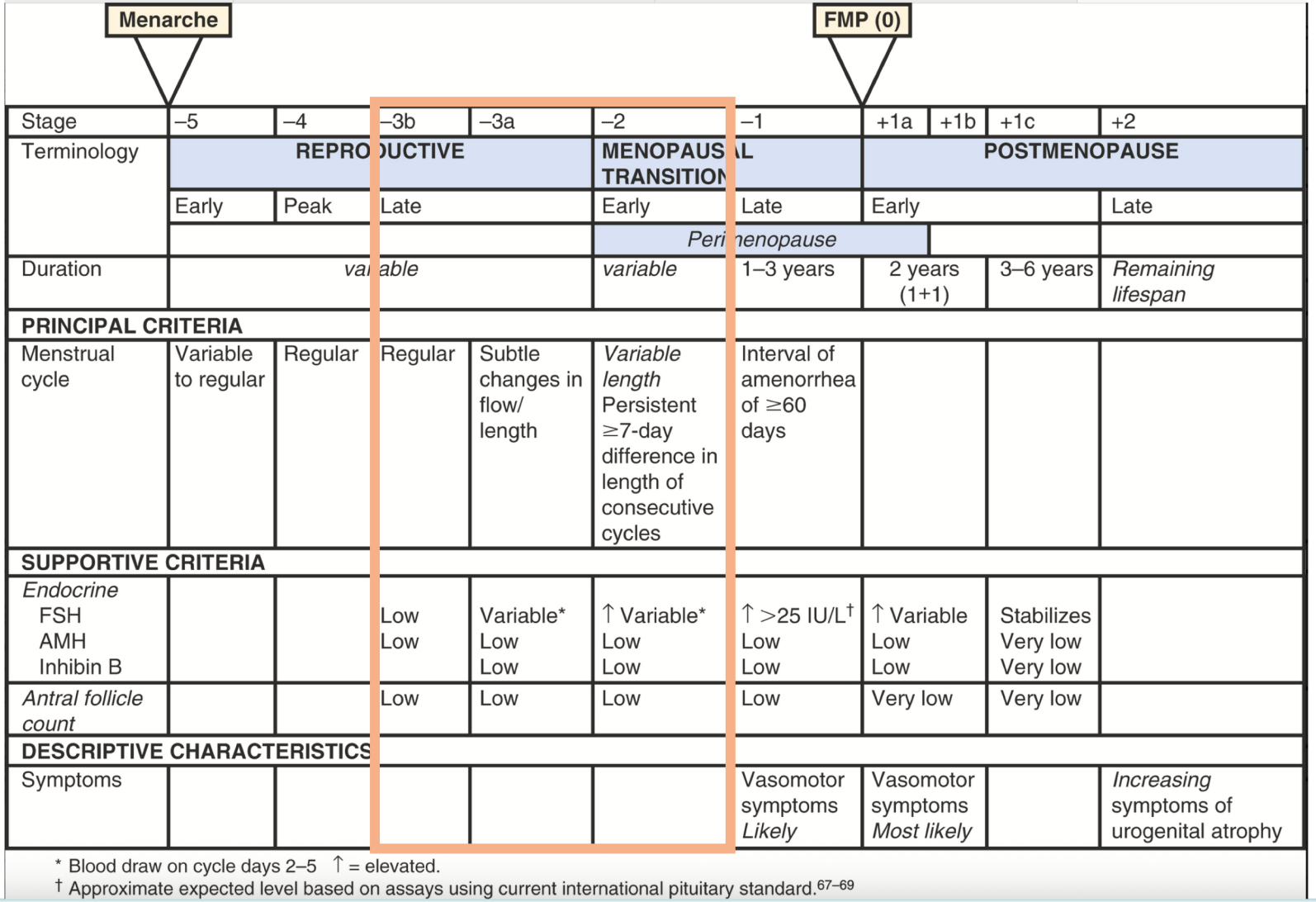
Menopausal Transition

STRAW +10 stages



	Menarche					FMP (0)				
Stage	–5	–4	–3b	–3a	–2	–1	+1a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1–3 years	2 years (1+1)		3–6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
Menstrual cycle	Variable to regular	Regular	Regular	Subtle changes in flow/ length	*Variable length* Persistent ≥7-day difference in length of consecutive cycles	Interval of amenorrhea of ≥60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 IU/L† Low Low	↑ Variable Low Low		Stabilizes Very low Very low	
Antral follicle count			Low	Low	Low	Low	Very low		Very low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2–5 ↑ = elevated.
† Approximate expected level based on assays using current international pituitary standard.[67–69]

- Yen & Jaffe's Reproductive Endocrinology, Ninth Edition - Modified from Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. J Clin Endocrinol Metab. 2012;97[4]:1159–1168

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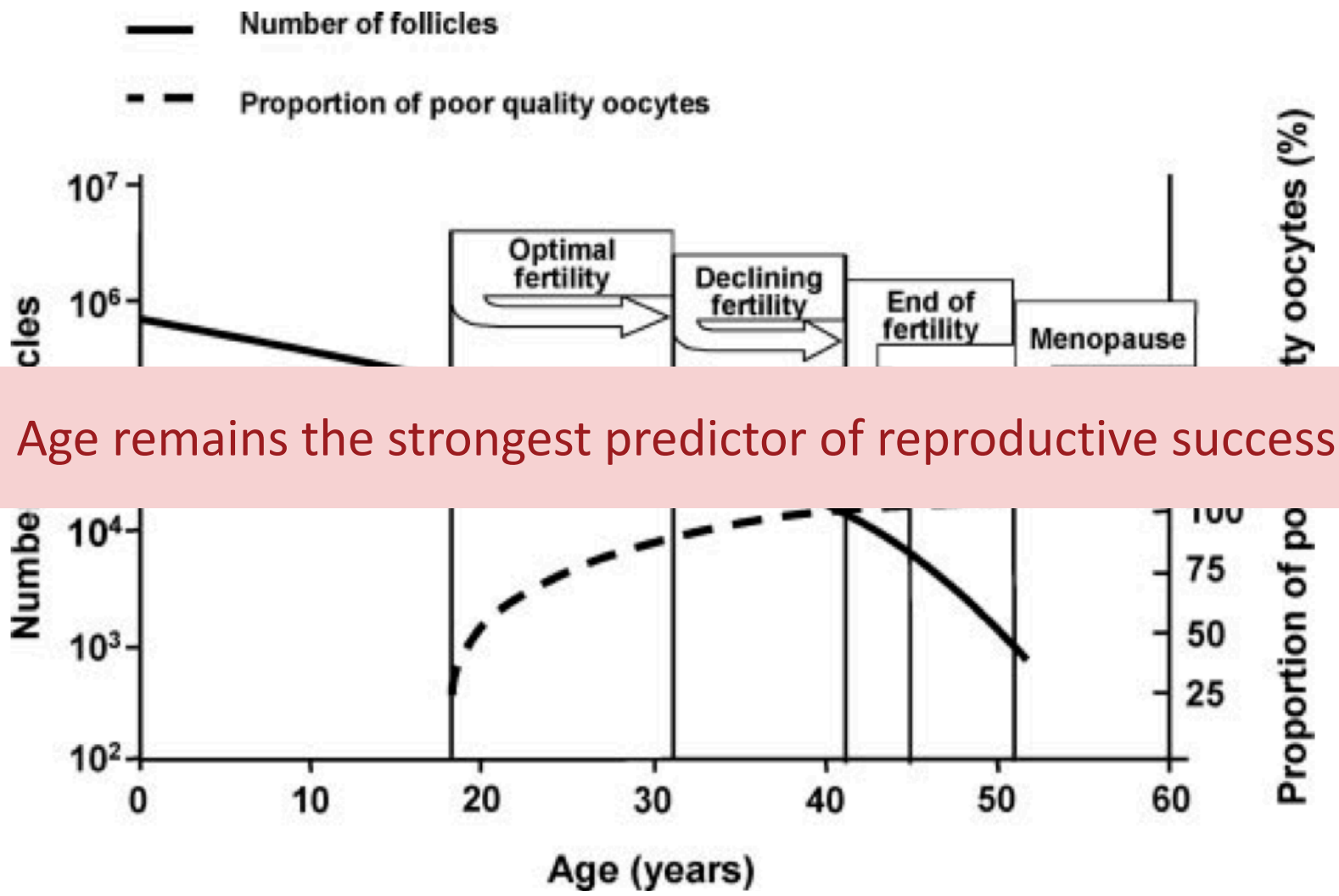
Fertility Decline



Age remains the strongest predictor of reproductive success

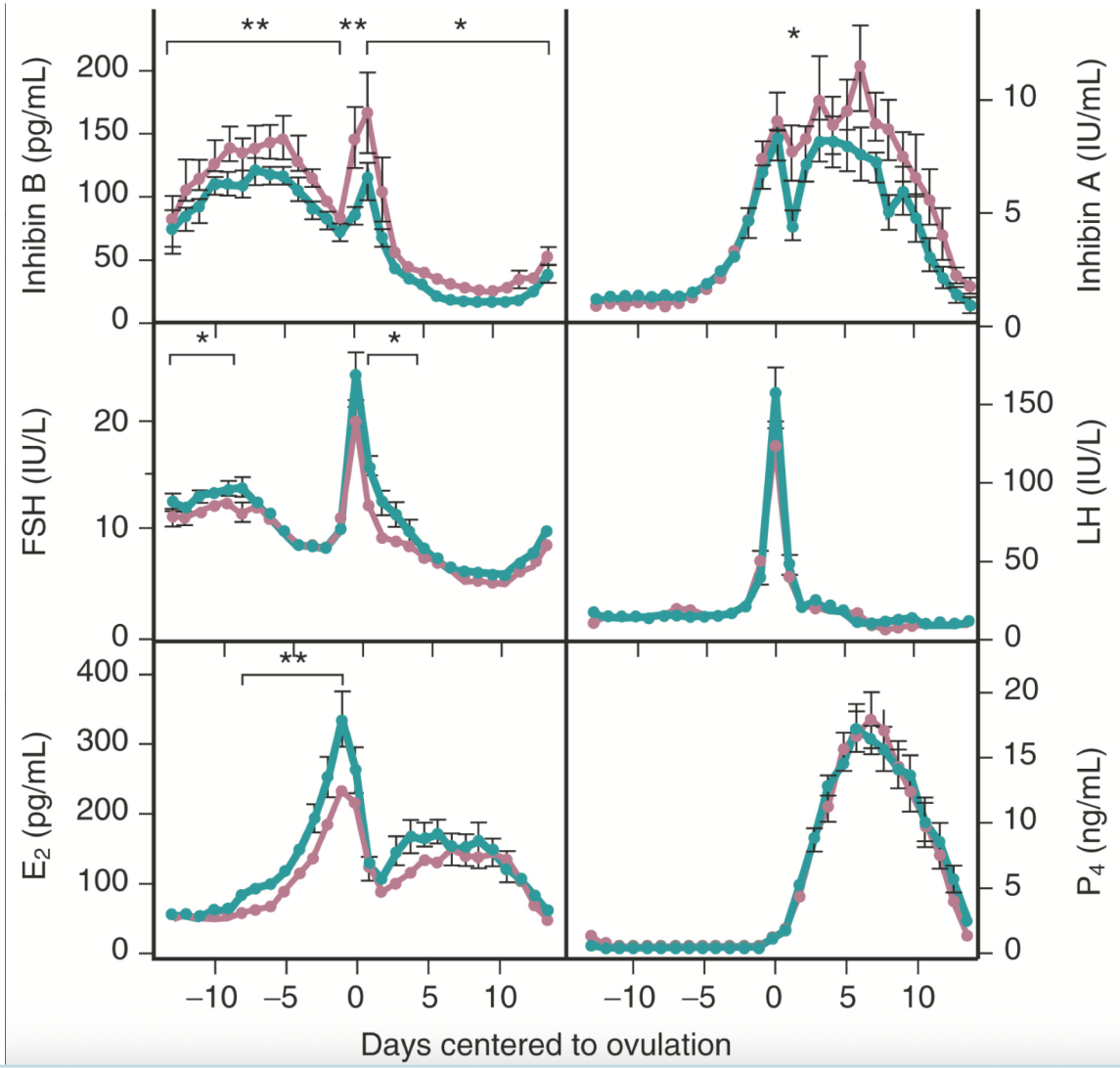
- Broekmans FJ, Soules MR, Fauser BC. Ovarian aging: mechanisms and clinical consequences. Endocr Rev. 2009 Aug;30(5):465-93. doi: 10.1210/er.2009-0006

The age, too old…

Hormonal Levels

20 to 34 years old

35 to 46 years old



Key change after 35

Drop in inhibin B → weaker FSH feedback → early FSH rise

Estradiol

May peak higher mid-cycle (due to increased FSH stimulating remaining follicles)

Luteal function

Largely preserved

- Yen & Jaffe's Reproductive Endocrinology, Ninth Edition; Modified from Welt CK, McNicholl DJ, Taylor AE, Hall JE: Female reproductive aging is marked by decreased secretion of dimeric inhibin. J Clin Endocrinol Metab. 1999;84:105–111

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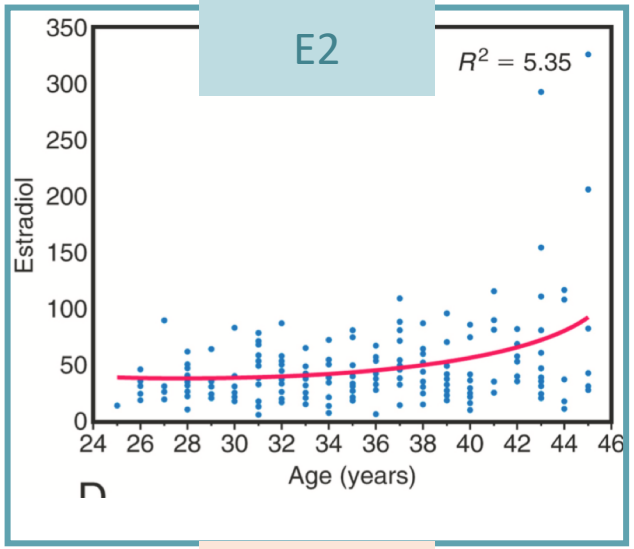
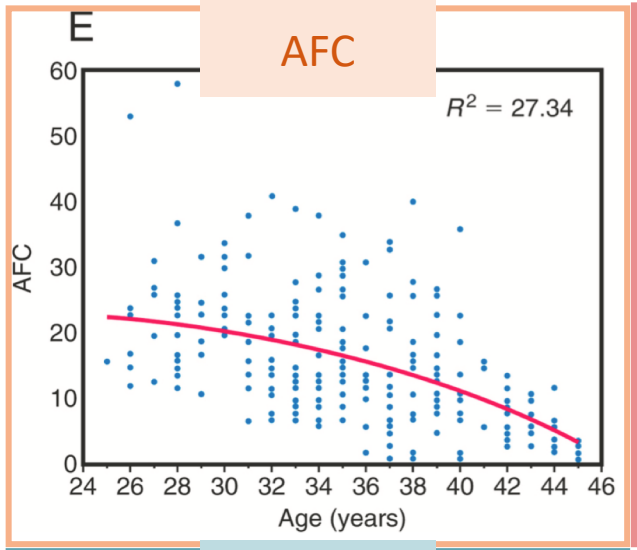
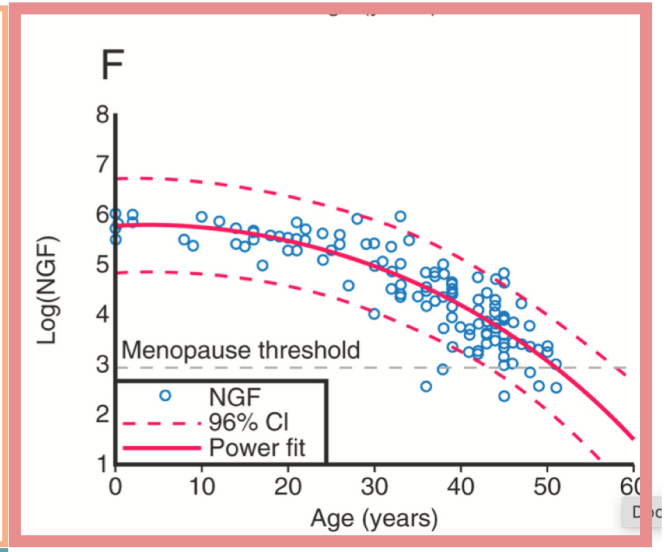
Hormonal Levels

E2

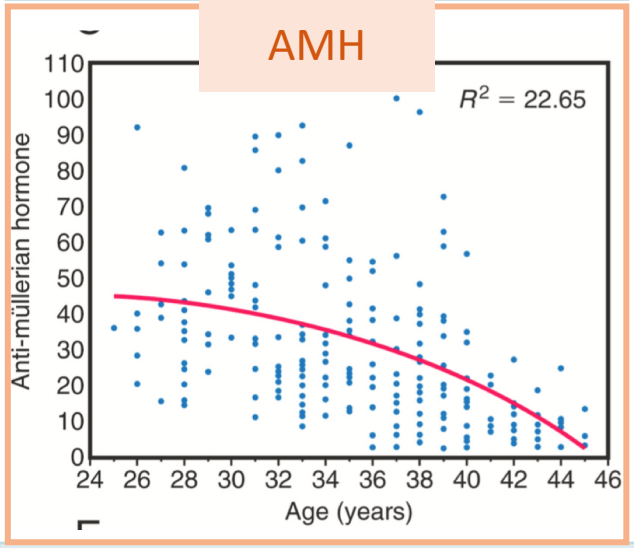


AFC

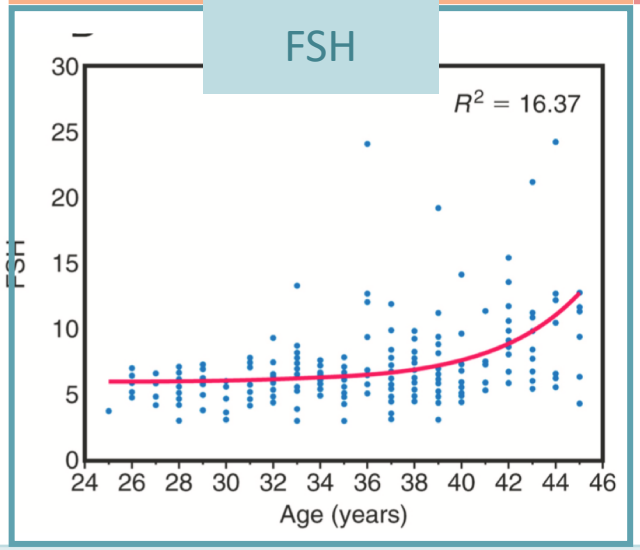




AMH



FSH



AFC & AMH

- Closely follow follicle loss pattern
- Decline accelerates from mid-30s

FSH & E_2

- Increase later, after major follicle depletion
- Reflect endocrine adaptation

- Yen & Jaffe's Reproductive Endocrinology, Ninth Edition - Modified from Rosen MP, Johnstone E, McCulloch CE, et al. A characterization of the relationship of ovarian reserve markers with age. Fertil Steril. 2012;97:238–243.

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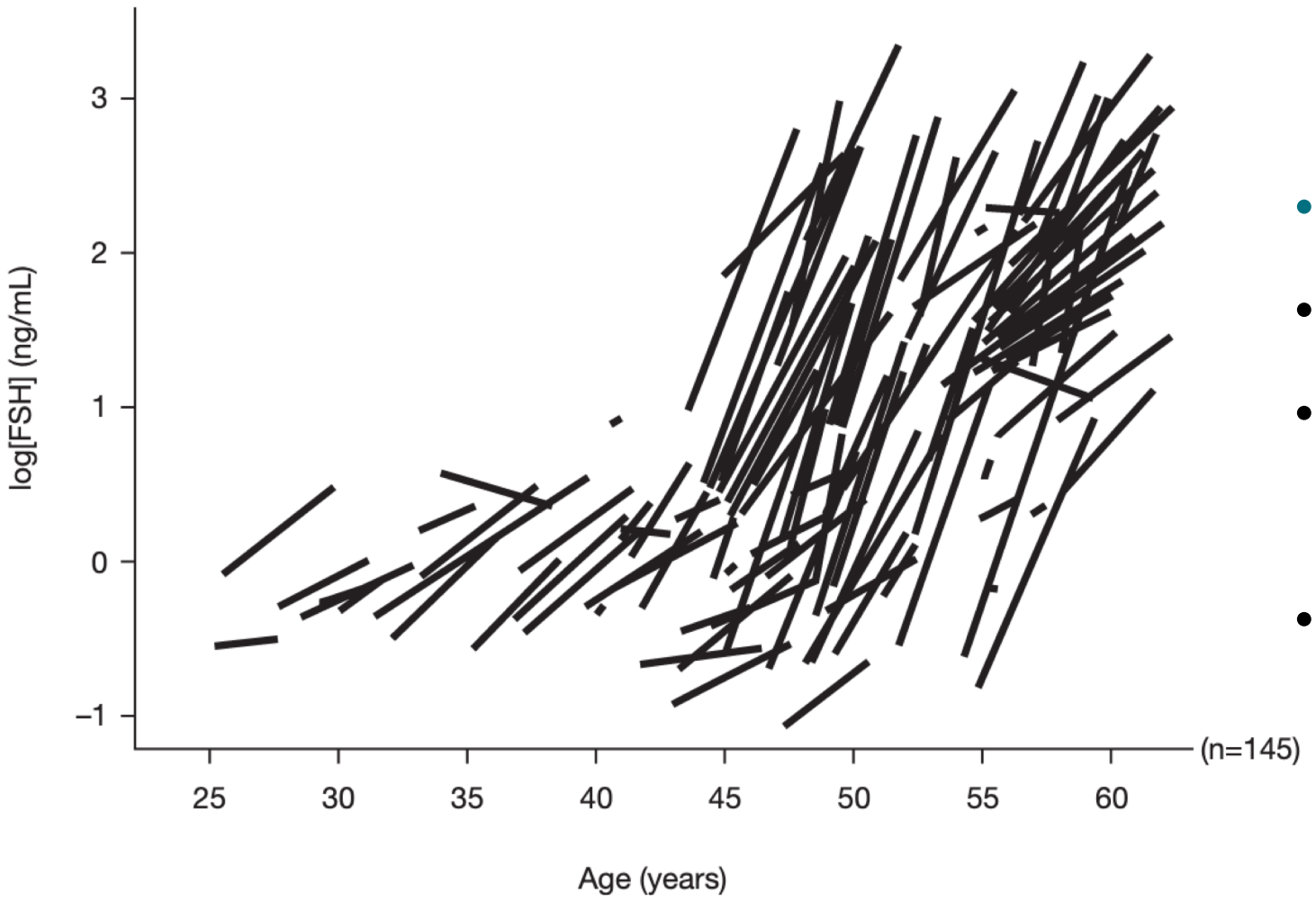
FSH Trajectories



- **Individual FSH trajectories over time**
- Gradual rise in late 30s–early 40s
- Sharp increase after +/-45 → perimenopausal transition
- Wide variability: early vs late changes

- Ferrell RJ, O'Connor KA, Holman DJ, Brindle E, Miller RC, Rodriguez G, Simon JA, Mansfield PK, Wood JW, Weinstein M. Monitoring reproductive aging in a 5-year prospective study: aggregate and individual changes in luteinizing hormone and follicle-stimulating hormone with age. Menopause. 2007 Jan-Feb;14(1):29-37. doi: 10.1097/01.gme.0000227859.50473.20
- Alviggi C, Humaidan P, Howles CM, Tredway D, Hillier SG. Biological versus chronological ovarian age: implications for assisted reproductive technology. Reprod Biol Endocrinol. 2009 Sep 22;7:101. doi: 10.1186/1477-7827-7-101

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HPO Axis

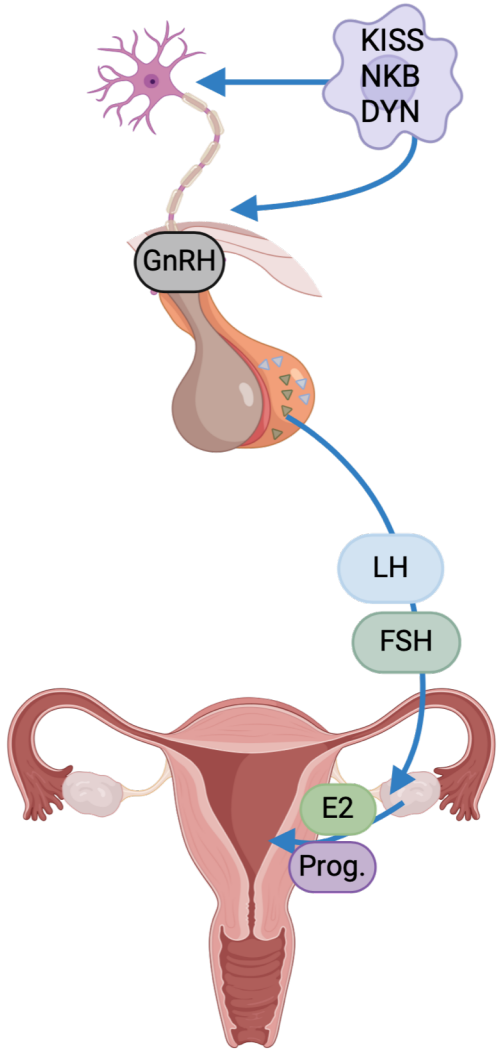
Underlying cause: Dysfunction of the hypothalamic–pituitary–ovarian axis

Neurotransmitter shifts:

- ↓ Glutamate → less excitatory input to GnRH neurons
- ↑ GABA → stronger inhibitory tone

KNDy neurons (kisspeptin, neurokinin B, dynorphin):

- Altered gene expression postmenopause
- Disrupts GnRH pulse generation



- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Figure created with BioRender.com

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Altered hypothalamic-pituitary signaling: GnRH, LH, FSH secretion changes

FSH

- Rises earlier and more markedly with age
- Isoforms become more glycosylated → lower receptor affinity → reduced biological effectiveness

LH

- Lulses widen, surge amplitude declines
- Isoforms shift to more sialylated, less sulfonated forms → decreased biological activity → impaired steroidogenesis and androgen production

• Longo M, Liuzzi F, De Carlini S, La Marca A. The role of LH in follicle development: from physiology to new clinical implications. Reprod Biol Endocrinol. 2025 Feb 10;23(Suppl 1):22. doi: 10.1186/s12958-025-01353-8

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Ovarian Aging

Telomere

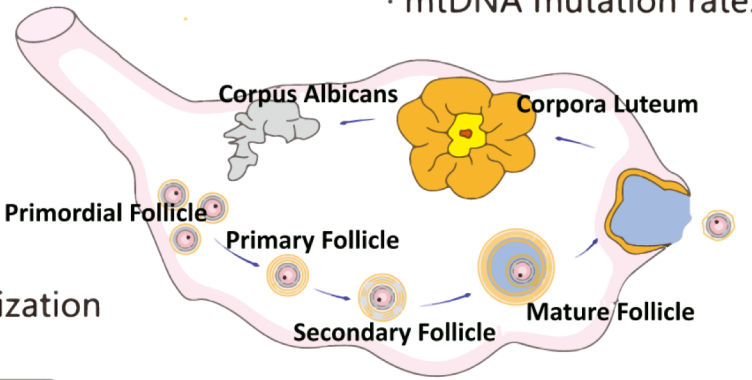
· telomere is shortened with a decreased level of telomerase and other telomere-associated protein

Mitochondria

· a decrease in certain material active in mitochomdria metablism
· mtDNA copy number decreases around ovulation and cleavage stage and increases thereafter
· mtDNA mutation rate: controversy

Oxidative Sress

· ROS accumulates with a diminished antioxidants, triggering downstream cascades
· AGEs accumulates, which might compromise vascularization



Aneuploidy

· a loss of cohesion in both homologous chromosomes and sister chromatids
· spindle disability
· a lax supervision of meiotic check point

Apoptosis and Autophagy

· Apoptosis: controversy
· Autophagy: a decrease in autophagic function

DNA Damage

· DSBs and SSBs accumulate with a decreased expression level of members of repairment pathway

Protein Homeostasis

· accumulation of misfolded, mislocalized and aggregated proteins, inducing UPR

- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z

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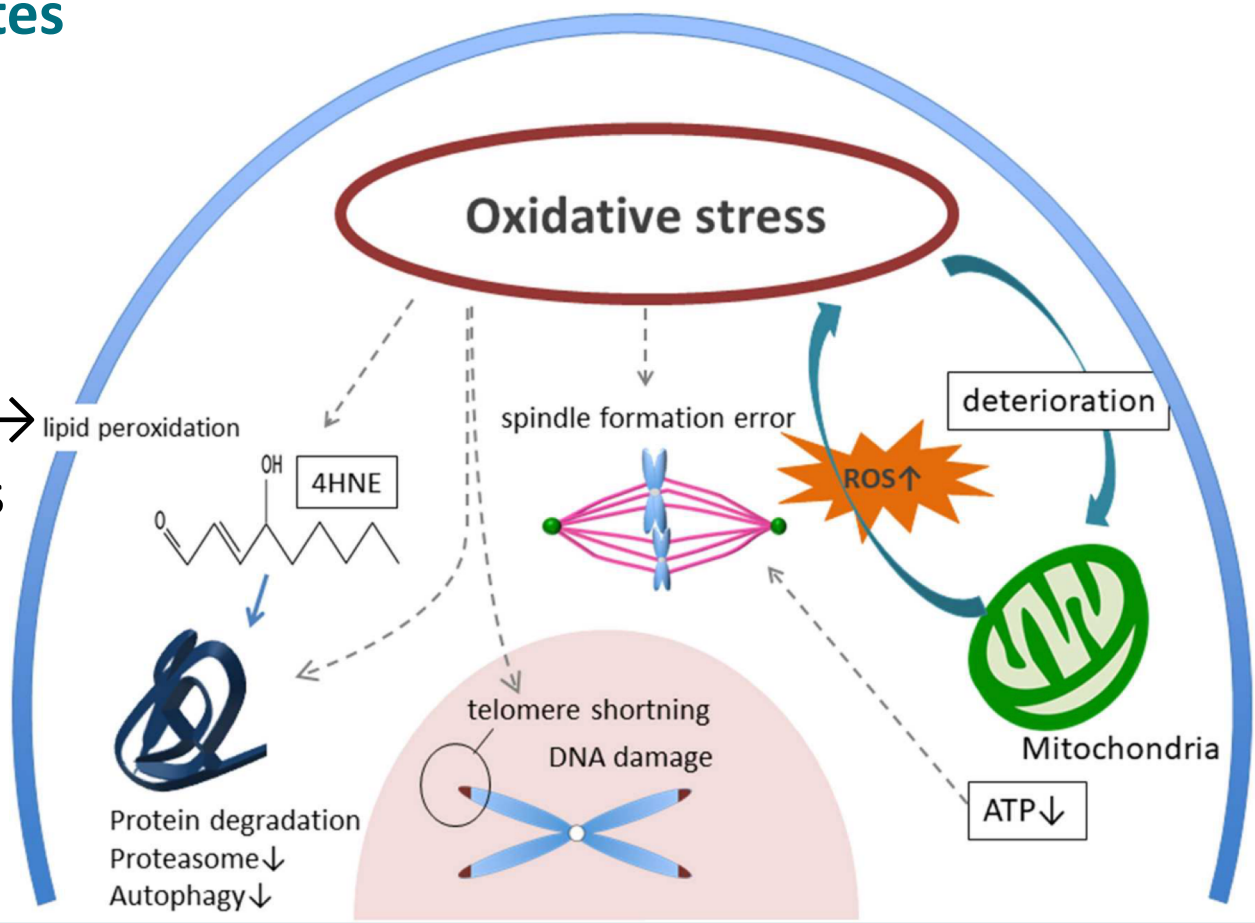
Oxidative Stress

Antioxidant defenses weaken within oocytes

→ ROS accumulation

- Damage to proteasome and autophagy systems
- Creates a hostile follicular environment → impairs oocyte maturation and increases meiotic errors
- Contributes to telomere shortening and amplifies cellular aging processes



- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Sasaki H, Hamatani T, Kamijo S, Iwai M, Kobanawa M, Ogawa S, Miyado K, Tanaka M. Impact of Oxidative Stress on Age-Associated Decline in Oocyte Developmental Competence. Front Endocrinol (Lausanne). 2019 Nov 22;10:811. doi: 10.3389/fendo.2019.00811

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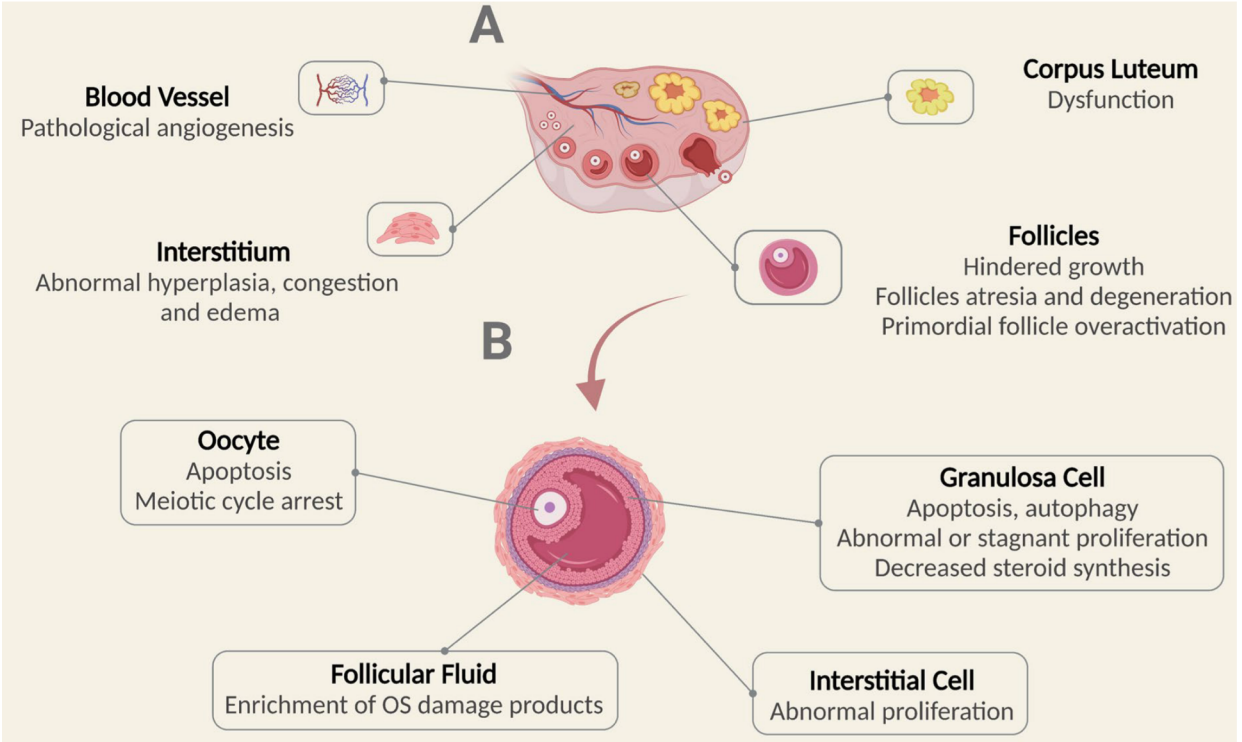
Oxidative Stress

- **Vascular damage**: ROS impair ovarian blood vessels, reducing oxygen and nutrient supply
- **Granulosa cell apoptosis**: Leads to follicular atresia and disrupted hormone production
- **Stromal and interstitial injury**: Alters structural integrity and signaling within the ovary
- **Inflammation cascade**: ROS activate inflammasomes and NF-κB, amplifying chronic inflammation
- **Follicular fluid imbalance**: Increased oxidative products disrupt the microenvironment for oocyte maturation



Oxidative stress transforms the ovary into a hostile environment for follicle development

- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Yan F, Zhao Q, Li Y, Zheng Z, Kong X, Shu C, Liu Y, Shi Y. The role of oxidative stress in ovarian aging: a review. J Ovarian Res. 2022 Sep 1;15(1):100. doi: 10.1186/s13048-022-01032-x

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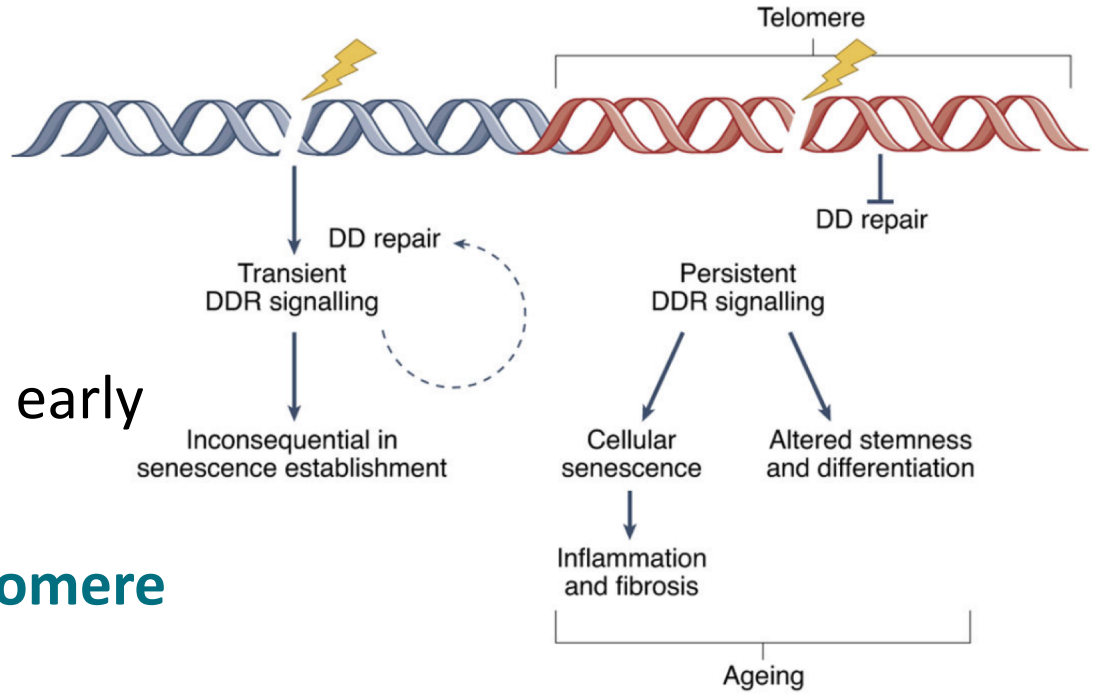
Telomere Shortening

- **Shorter telomeres** and **lower telomerase** in oocytes/granulosa cells
- **Estrogen deficiency** accelerates attrition
- Short telomeres → **higher aneuploidy**, lower implantation
- Linked to **premature ovarian insufficiency** and early infertility
- IVF patients often show **reduced leukocyte telomere length**



- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Rossiello F, Jurk D, Passos JF, d'Adda di Fagagna F. Telomere dysfunction in ageing and age-related diseases. Nat Cell Biol. 2022 Feb;24(2):135-147. doi: 10.1038/s41556-022-00842-x

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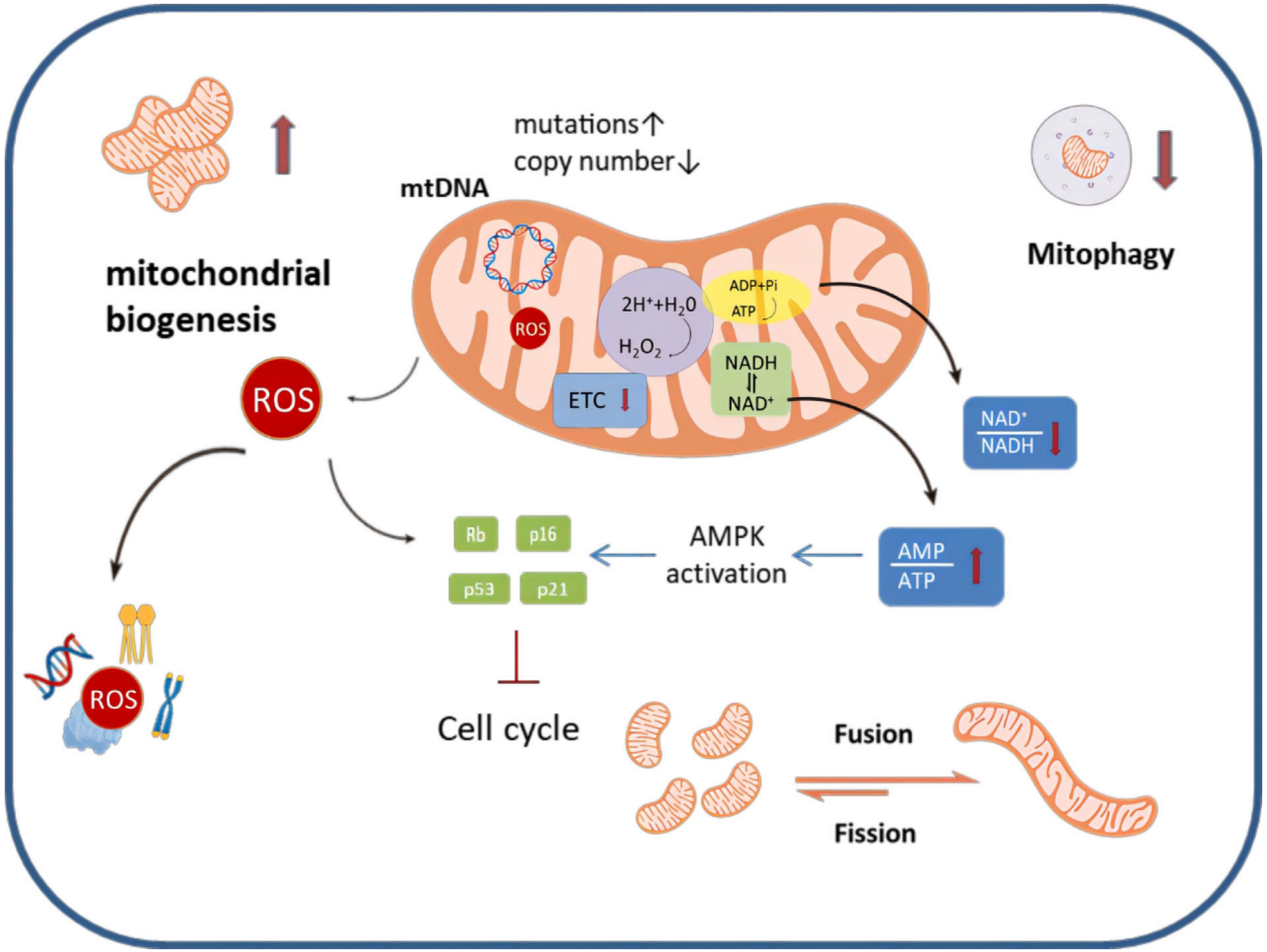
Mitochondrial Dysfunction

- Decreased **ATP production** → spindle assembly errors
- Modification of **mtDNA** copy number and mutation accumulation
- NAD^+ decline and **oxidative phosphorylation impairment** → compromise energy balance



- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Wang ZH, Wang ZJ, Liu HC, Wang CY, Wang YQ, Yue Y, Zhao C, Wang G, Wan JP. Targeting mitochondria for ovarian aging: new insights into mechanisms and therapeutic potential. Front Endocrinol (Lausanne). 2024 Jun 17;15:1417007. doi: 10.3389/fendo.2024.1417007

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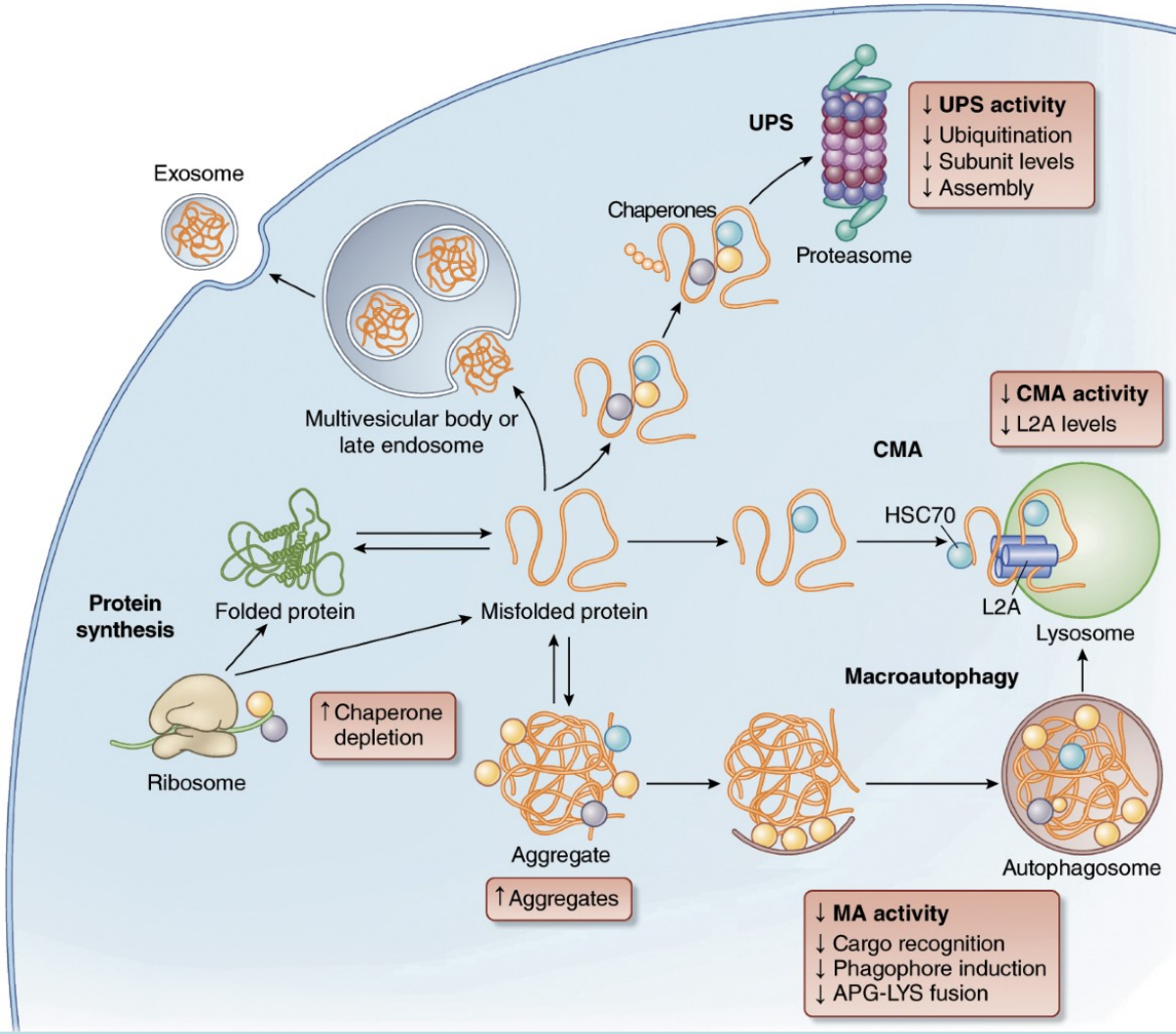
Protein Homeostasis Failure

- **ROS** → Disrupts protein quality control (**Impaired proteostasis**)
- Chaperones and proteasomes weaken
- Unfolded protein response & accumulation of **misfolded proteins** (e.g., 4-HNE adducts) → aggregates → impair cellular function and accelerate follicular decline



- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Kaushik S, Cuervo AM. Proteostasis and aging. Nat Med. 2015 Dec;21(12):1406-15. doi: 10.1038/nm.4001

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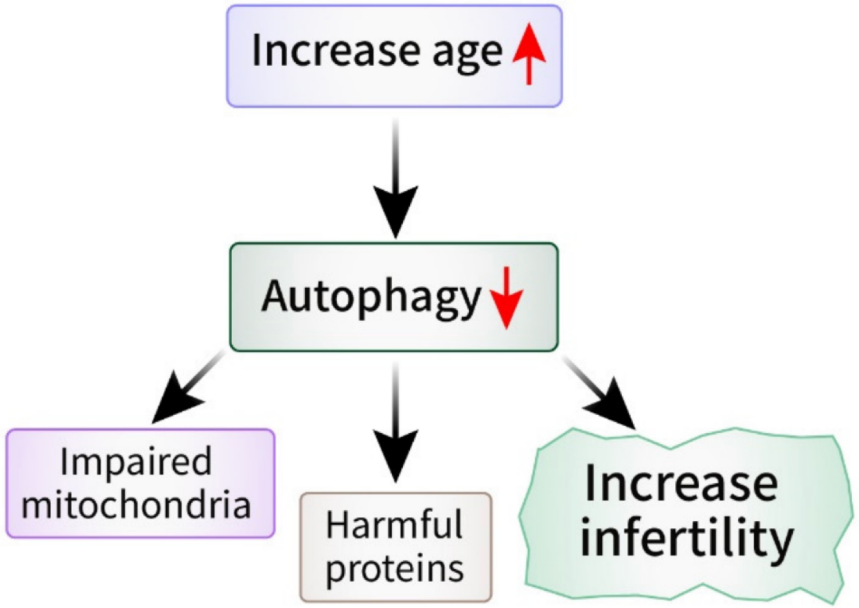
Apoptosis & Autophagy

- **Follicle survival** depends on a fine balance between apoptosis and autophagy
- **Autophagy** protects cells by recycling damaged organelles and maintaining homeostasis
- Age → ↓ Activity

  → **Accumulation of dysfunctional mitochondria**

  → **Build-up of altered proteins**

  → **Accelerated ovarian aging**



- Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 6;16(1):67. doi: 10.1186/s13048-023-01151-z
- Harrath AH, Rahman MA, Bhajan SK, Bishwas AK, Rahman MDH, Alwasel S, Jalouli M, Kang S, Park MN, Kim B. Autophagy and Female Fertility: Mechanisms, Clinical Implications, and Emerging Therapies. Cells. 2024 Aug 14;13(16):1354. doi: 10.3390/cells13161354.

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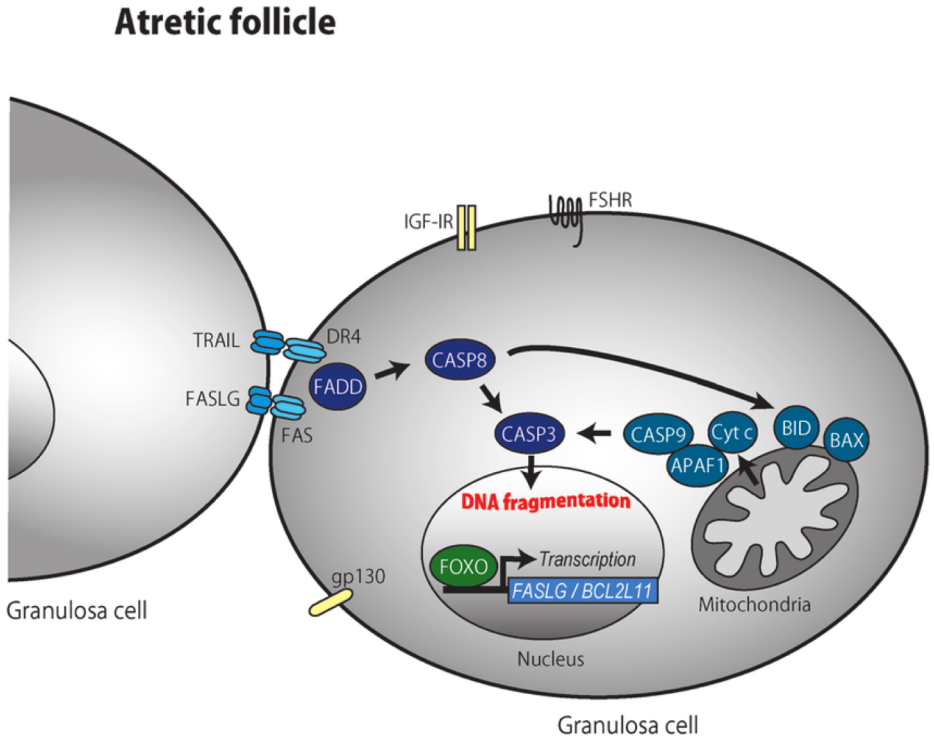
Apoptosis & Autophagy

- **Apoptosis** → main mechanism eliminating most follicles through atresia
- Age → ↑ Activity
- Granulosa cells show a **unique epigenetic aging pattern** with more age-related methylation changes than other tissues
- **Granulosa cell apoptosis** affects follicle survival



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- **Mural granulosa cell** (MGC) **apoptosis** affects follicle survival → marker of poor ovarian response

Comparison of apoptosis of MGCs in different age groups				
Parameters	**<30 (n=64)**	**30-37 (n=70)**	**≥37 (n = 30)**	**P value**
MGCs early apoptosis rate (%)	0.45 (0.20-1.00)	0.62 (0.25-1.46)	1.30 (0.535-2.40)	<0.0001
MGCs late apoptosis rate (%)	2.08 (0.29-5.67)	2.26 (0.42-4.81)	6.40 (2.33-15.70)	<0.05
MGCs total apoptosis rate (%)	2.85 (0.83-6.42)	2.77 (1.00-6.69)	6.91 (3.92-17.05)	<0.0005

164 women (21–46 years) undergoing IVF cycle, one transfer (fresh or frozen)

- Granulosa cells apoptosis correlated with **age**, worse ovarian response, fewer egg and embryos
- Early apoptosis rate of MGC significantly higher in **non pregnant group**

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- Fan Y, Chang Y, Wei L, Chen J, Li J, Goldsmith S, Silber S, Liang X. Apoptosis of mural granulosa cells is increased in women with diminished ovarian reserve. J Assist Reprod Genet. 2019 Jun;36(6):1225-1235. doi: 10.1007/s10815-019-01446-5

…the eggs too few

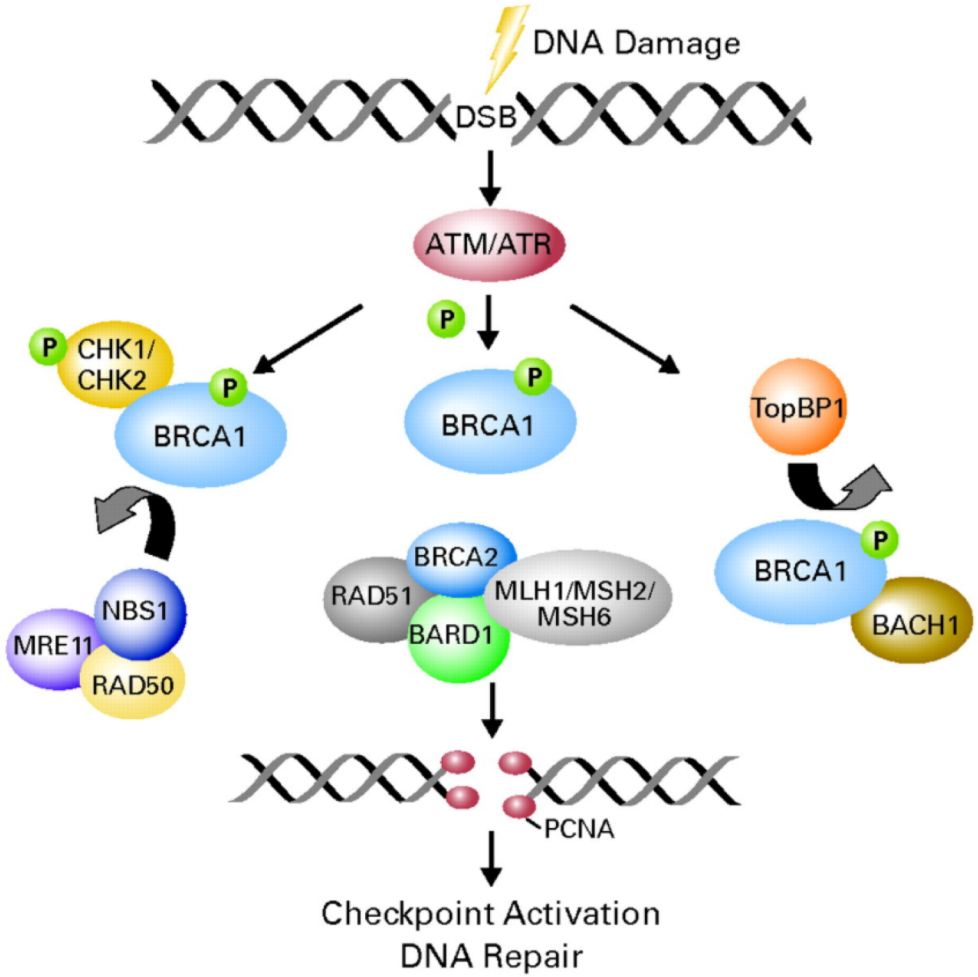
Primordial follicles remain arrested for decades

→ ↑ **oocyte vulnerability** to ROS and external stressor:

- Accumulation of **double-strand breaks** (DSBs)
- Decline in **homologous recombination repair** (BRCA1, ATM, RAD51)

→ Increased susceptibility to **aneuploidy**

DNA Damage



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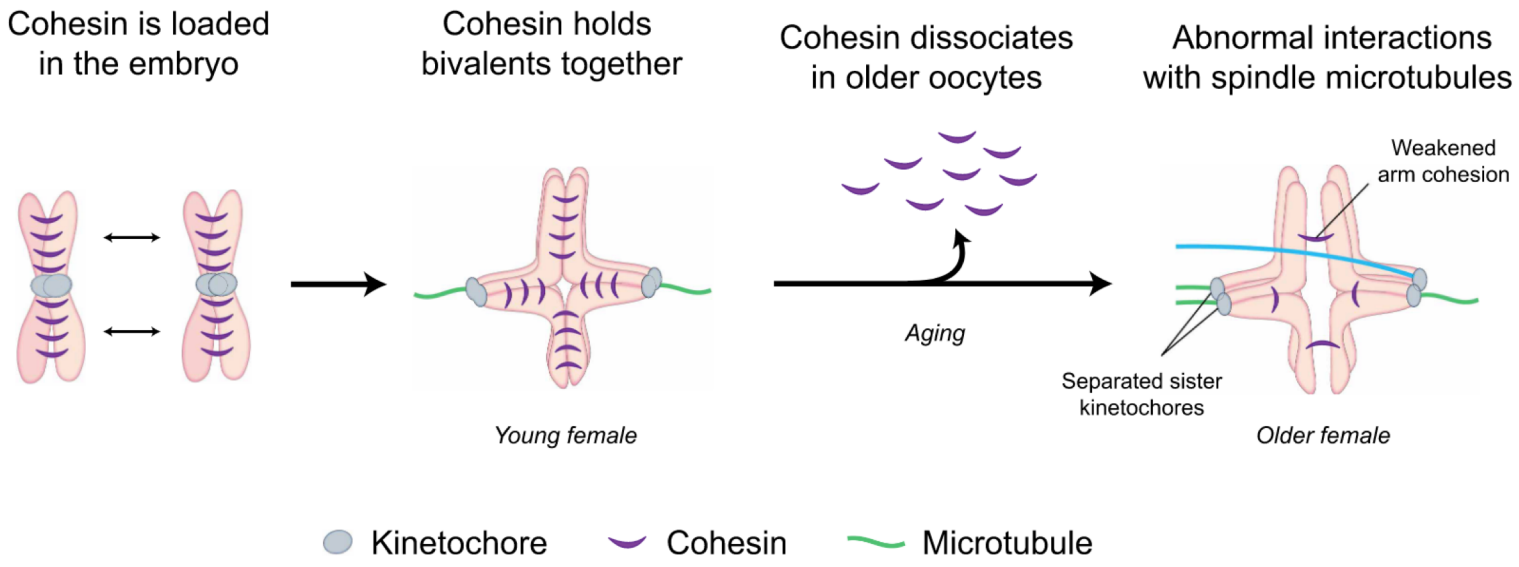
Aneuploidy

- **Cohesin loss** and **spindle instability**
- Cohesin loss with age → weakens chromatid links → premature separation → faulty microtubule attachments
- Combined with spindle defects → segregation errors → poor fertility outcomes in older oocytes



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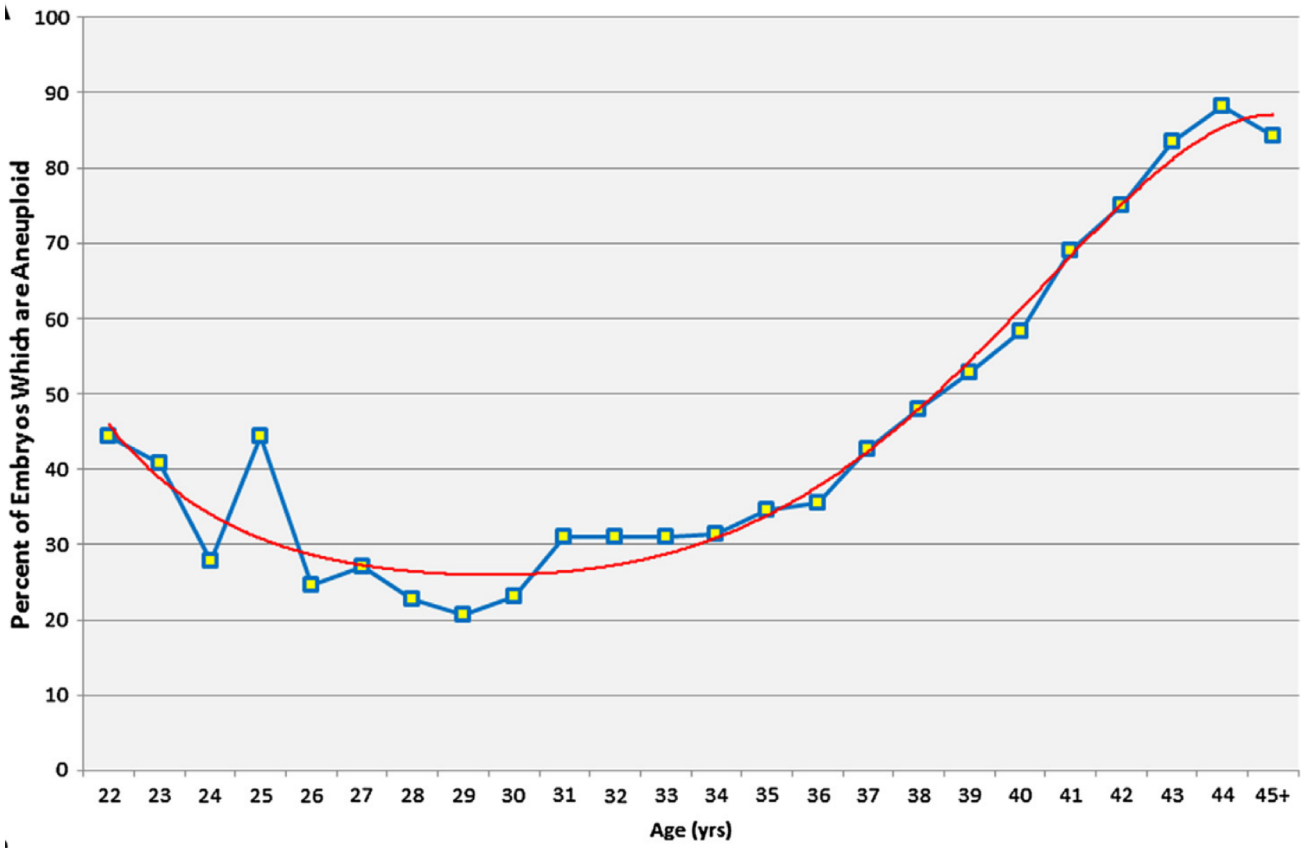
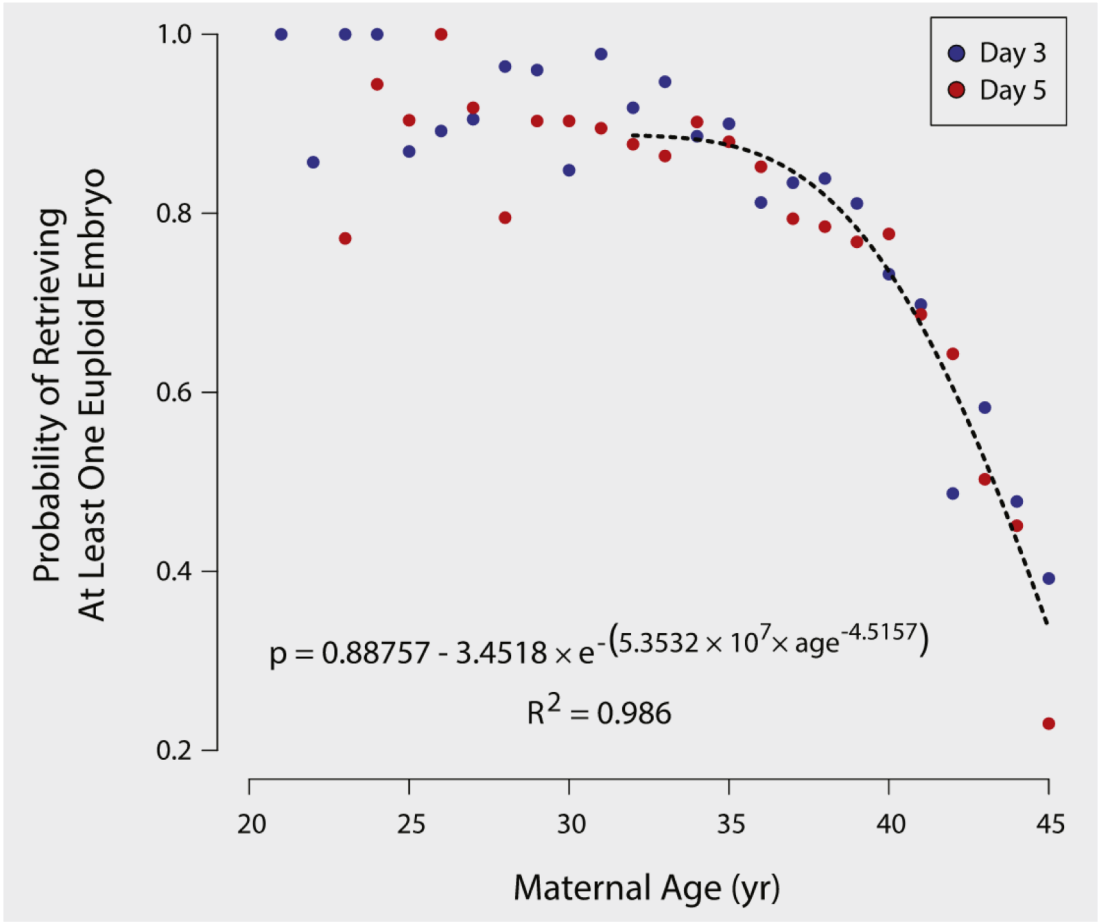
…the eggs too few

Aneuploidy





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- Demko ZP, Simon AL, McCoy RC, Petrov DA, Rabinowitz M. Effects of maternal age on euploidy rates in a large cohort of embryos analyzed with 24-chromosome single-nucleotide polymorphism-based preimplantation genetic screening. Fertil Steril. 2016 May;105(5):1307-1313. doi: 10.1016/j.fertnstert.2016.01.025

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Poor ovarian response

A heat-map presenting the number of frozen mature oocytes by age and percentile

Age (Years)	Centiles												
	5	10	20	25	30	40	50	60	70	75	80	90	95
30	8	9	11	12	13	14	15	17	19	20	21	25	28
31	6	7	9	10	10	12	13	14	16	17	19	23	26
32	5	6	8	8	9	10	12	13	15	16	18	22	26
33	5	6	7	8	9	10	11	13	15	16	17	22	26
34	5	6	7	8	8	10	11	13	15	16	18	23	28
35	4	5	7	7	8	9	11	12	14	16	17	22	28
36	4	4	6	6	7	8	10	11	13	15	16	21	27
37	3	4	5	5	6	7	8	10	12	13	15	20	26
38	2	3	4	5	5	6	8	9	11	12	14	19	25
39	2	3	4	4	5	6	7	8	10	12	13	18	23
40	2	2	3	4	4	5	6	8	10	11	12	18	23
41	1	2	3	3	4	5	6	7	9	11	12	18	25

- Machtinger R, Tuval A, Hammerman A, Maman E, Nahum R, Orvieto R, Noah Hirsh M, Aizer A, Ziv Baran T. Age-Based Oocyte Yield in Elective Oocyte Cryopreservation: A Retrospective Cohort Study. Diagnostics (Basel). 2025

…the eggs too few

Poor ovarian response

Advanced maternal age

- Ovarian ageing
- Follicle endocrine milieu changes
- LH bioactivity ↓
- LH receptor activity ↓
- Steroidogenesis ↓

Reduced gonadotropin ACTION

- Wide et al. J Clin Endocrinol Metab. 2007;92:4410-4417
- Vihko et al. Eur J Endocrinol. 1996;134(3):357-61
- Zumoff et al. J Clin Endocrinol Metab. 1995;80:1429-30
- Bosch et al. Fertil Steril. 2011 Mar 1;95(3):1031-6
- Humaidan et al. Reprod Biomed Online. 2004 Jun;8(6):635-43
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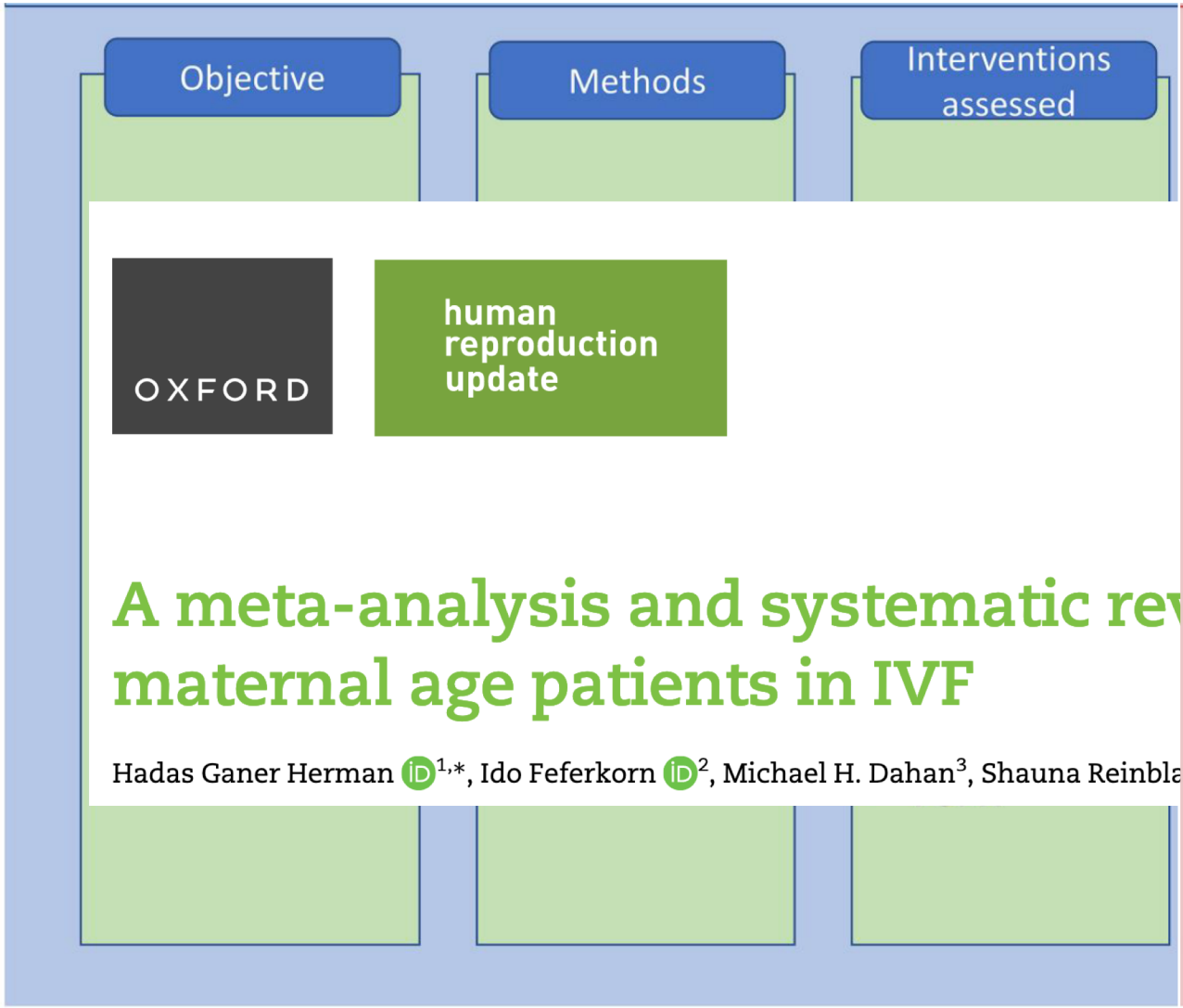
…the eggs too few

Therapeutic strategies



Results

- 151 studies included
- Variable quality of evidence
- Advanced maternal age – >35 years common to all studies

Results

- No advantage to specific stimulation strategies, FSH type, and freeze all. No benefit to the addition of LH to FSH in our meta-analysis
- No good evidence for routine ICSI
- Lower rate of live births with routine assisted hatching in our meta-analysis
- Similar live birth rates with PGT-A in our meta-analysis

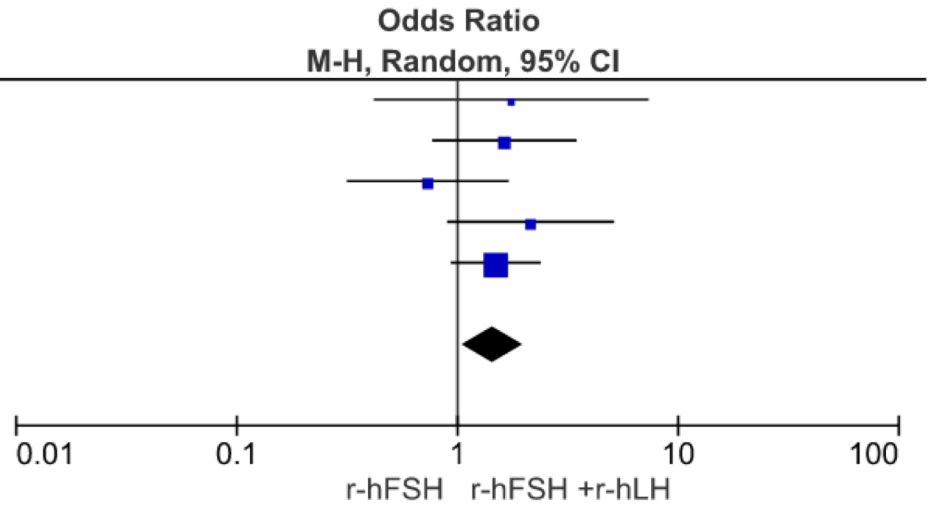
- Ganer Herman H, Feferkorn I, Dahan MH, Reinblatt S, Demirtas E, Buckett W. A meta-analysis and systematic review of advanced maternal age patients in IVF. Hum Reprod Update. 2025 Nov 1;31(6):626-642. doi: 10.1093/humupd/dmaf020

Forest plot showing the effect of r-hFSH + r-hLH versus r-hFSH monotherapy in ovarian stimulation on **clinical pregnancy rates** between 35 and 40 years old

Study or Subgroup	r-hFSH + r-hLH Events	Total	r-hFSH Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Humaidan et al. 2004	7	21	4	18	5.1%	1.75 [0.42, 7.35]	2004
Marrs et al. 2004	27	65	17	56	18.6%	1.63 [0.77, 3.46]	2004
Nyboe Andersen et al. 2008	14	49	18	51	14.8%	0.73 [0.32, 1.71]	2008
Matorras et al. 2009	17	63	10	68	13.9%	2.14 [0.90, 5.12]	2009
Bosch et al. 2011	57	170	43	170	47.7%	1.49 [0.93, 2.38]	2011
Total (95% CI)		**368**		**363**	**100.0%**	**1.45 [1.05, 2.00]**	
Total events	122		92				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.44$, df = 4 (P = 0.49); $I^2 = 0\%$

Test for overall effect: Z = 2.23 (P = 0.03)



• Conforti A, Esteves SC, Humaidan P, Longobardi S, D'Hooghe T, Orvieto R, Vaiarelli A, Cimadomo D, Rienzi L, Ubaldi FM, Zullo F, Alviggi C. Recombinant human luteinizing hormone co-treatment in ovarian stimulation for assisted reproductive technology in women of advanced reproductive age: a systematic review and meta-analysis of randomized controlled trials. Reprod Biol Endocrinol. 2021 Jun 21;19(1):91. doi: 10.1186/s12958-021-00759-4

…the eggs too few

Therapeutic strategies

Analysis of CoQ10 on clinical pregnancy rate

Subgroup	No. of studies	No. of women	Effect estimate OR (95% CI)	I^2	P
Dose					
30 mg/d	3	363	2.76 (1.78, 4.28)	0%	<0.00001
600 mg/d	2	225	1.62 (0.86, 3.05)	0%	0.13
1200 mg/d	1	78	1.24 (0.34, 4.45)	—	0.75
Treatment duration					
2 mo before the COS	2	225	1.62 (0.86, 3.05)	0%	0.13
3 mo before the COS	4	441	2.54 (1.68, 3.84)	0%	<0.0001
Population					
>35 y old with diminished ovarian reserve	3	356	2.07 (1.17, 3.65)	0%	0.01
>35 y old with suboptimal ovarian response	1	39	1.38 (0.29, 6.58)	—	0.68
<35 y old with diminished ovarian reserve	2	371	2.38 (1.26, 4.50)	46%	0.007

Low-dose CoQ10 (30 mg/day, 3 months) → possible ↑ clinical pregnancy
Effect mainly in **younger women with DOR**, less in older patients
Evidence low, live birth benefit unclear, methodological bias

- Shang Y, Song N, He R, Wu M. Antioxidants and Fertility in Women with Ovarian Aging: A Systematic Review and Meta-Analysis. Adv Nutr. 2024 Aug;15(8):100273. doi: 10.1016/j.advnut.2024.100273

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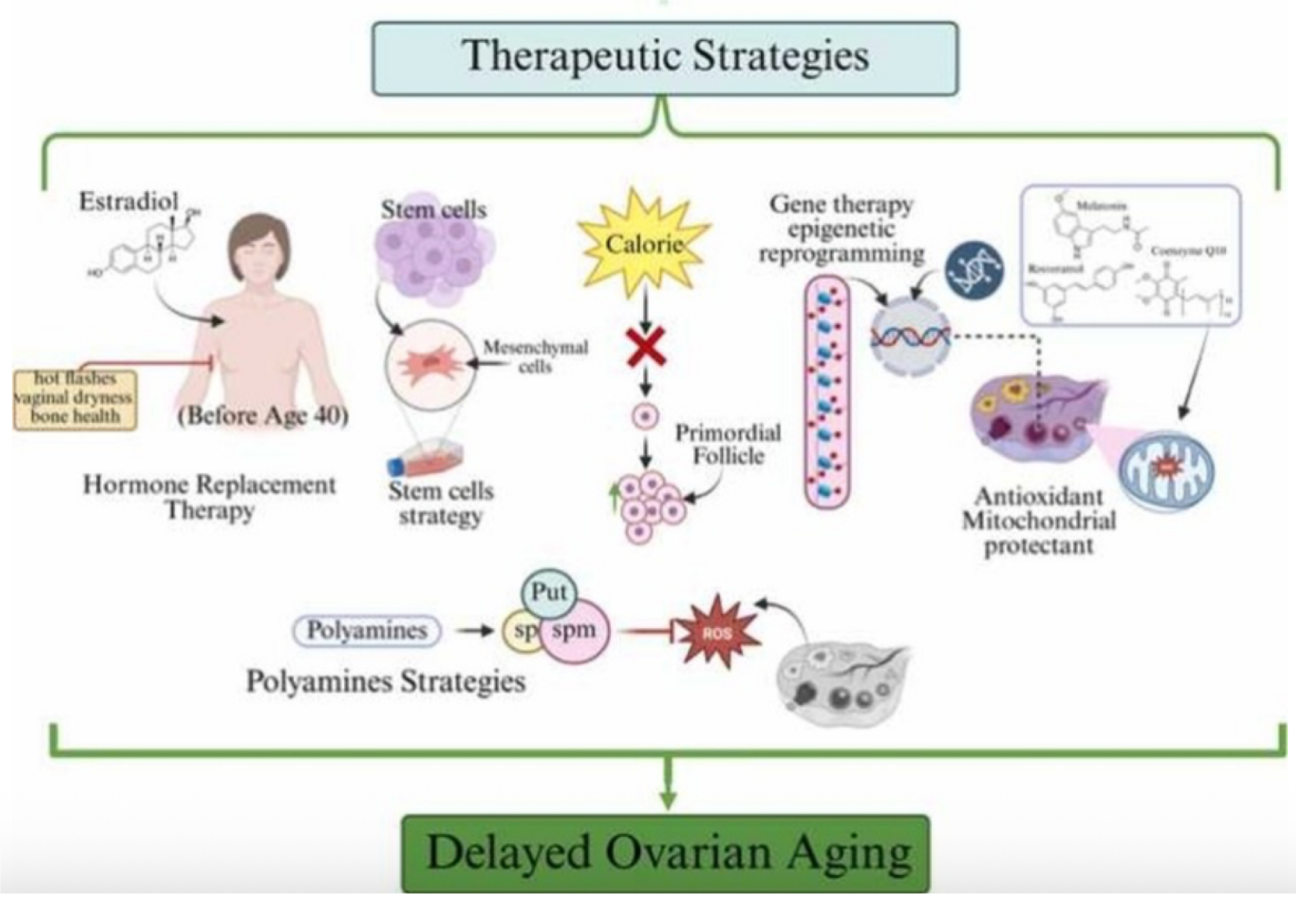
Therapeutic strategies

Emerging strategies to delay/reverse ovarian aging:

- Stem cell-based therapies
- Gene therapy
- Modulation of signaling pathways

Current status:

- Promising but experimental
- Require rigorous trials for efficacy, safety, and long-term impact



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- Mawet M, Perrier d'Hauterive S, Henry L, Potorac I, Kridelka F, Nisolle M, Pintiaux A. Restoration of Fertility in Patients with Spontaneous Premature Ovarian Insufficiency: New Techniques under the Microscope. J Clin Med. 2021 Nov 30;10(23):5647. doi: 10.3390/jcm10235647

Ovarian aging is multifactorial: genetic predisposition, epigenetic drift, mitochondrial dysfunction, and environmental stressors

Decline in oocyte quantity and quality accelerates after 35 years → reduced fertility and increased aneuploidy

Endocrine changes

- FSH ↑ with age, but glycosylation reduces receptor affinity → lower biological activity
- LH isoforms become less bioactive → impaired steroidogenesis and androgen production

Clinical impact

- Lower ovarian reserve (AMH, AFC) and diminished response to stimulation
- Higher IVF failure rates

Therapeutic strategies

- No effective therapeutic strategy
- Future directions: mitochondrial protection, stem cell-based therapies, oxidative stress reduction ?

Prevention: elective oocyte cryopreservation

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