TRAITEMENTS DE L'INFERTILITÉ ET RISQUES DE CANCER

O.Gervereau

CHU Tours

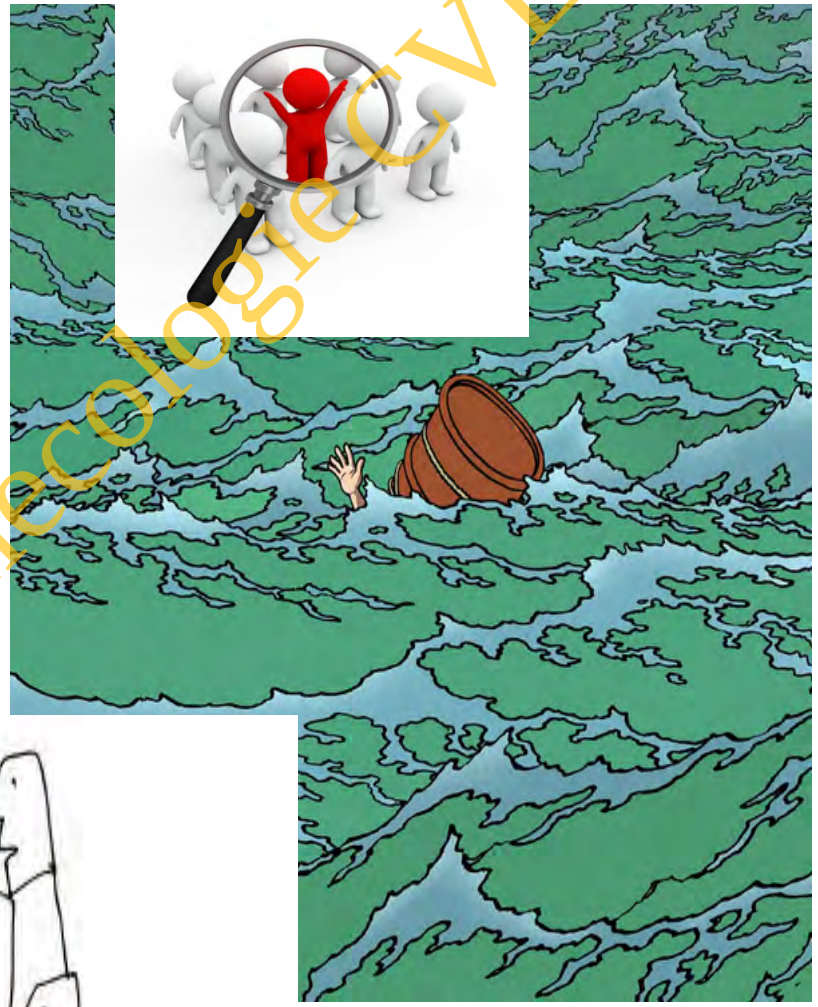
PRESCRIPTION EN CONSTANTE AUGMENTATION

- 1.2 à 2.3 % Enfants nés par techniques PMA
- Cycles FIV en constante augmentation

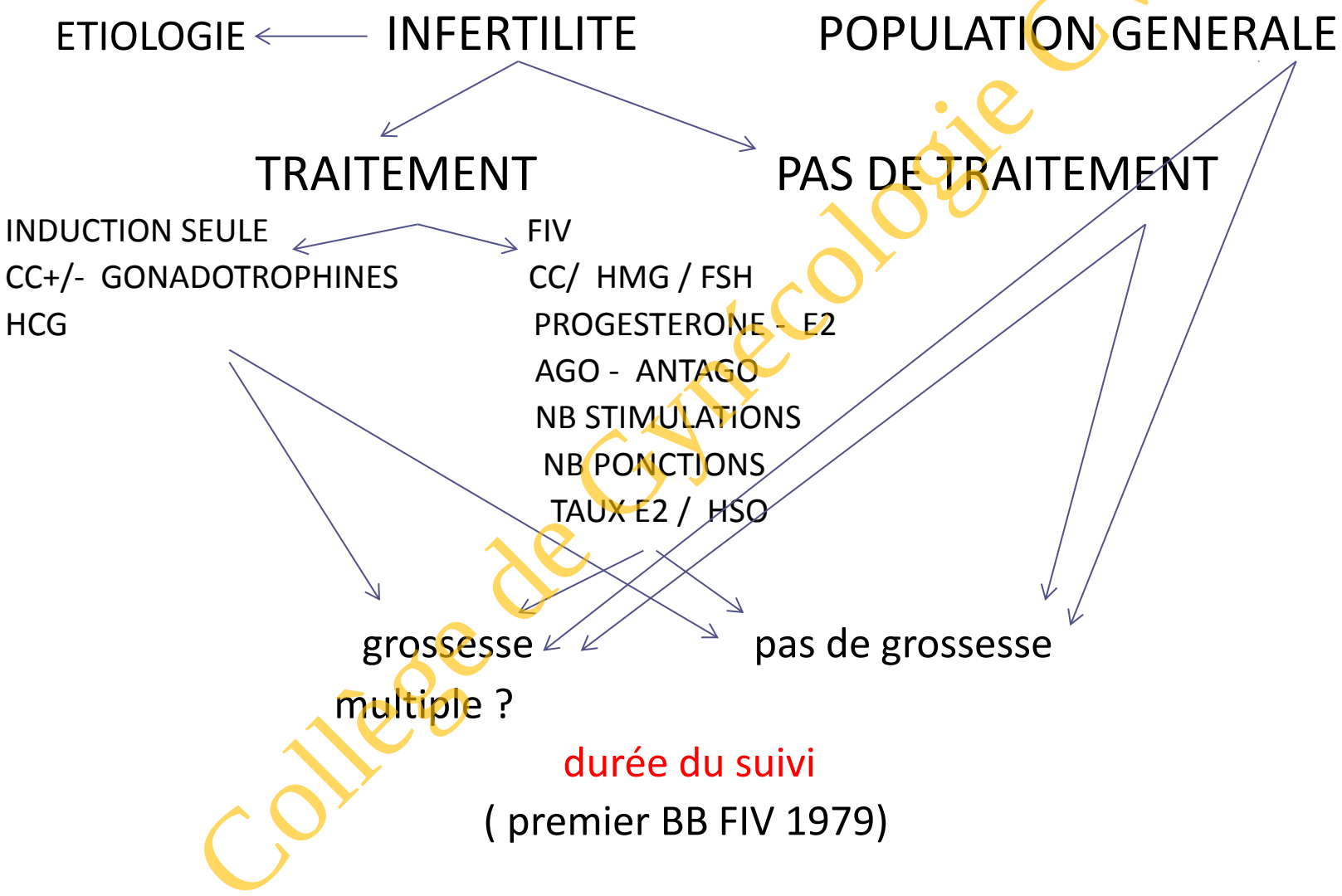
Tableau AMP1. Evolution de l'activité globale d'AMP entre 2007 et 2010

	2007	2008	2009	2010
Nombre de laboratoires d'AMP [nombre de laboratoires n'ayant pas transmis leur rapport] *	102 [1]	97 [11]	93 [4]	95 [1]
Nombre de centres clinico-biologiques [nombre de centres n'ayant pas transmis leur rapport] *	106 [0]	100 [5]	107 [0]	105 [1]
Nombre d'inséminations artificielles	54 618	53 365	57 301	60 357
Nombre de fécondations in vitro (FIV hors ICSI, ICSI, TEC)	67 438	68 150	74 415	78 987
Nombre total de tentatives**	122 056	121 515	131 716	139 344
* Nombre de centres ayant transmis un rapport annuel d'activité avant le gel de la base [Nombre de laboratoires ou centres n'ayant pas transmis le rapport annuel d'activité]				
** Tentatives : Cycles d'insémination artificielle (IIU, IIC) ; ponctions d'ovocytes dans le cadre des fécondations in vitro (FIV, ICSI) ; transferts d'embryons congelés (TEC)				

- Plus 10.000 cycles de FIV entre 2007 et 2010



BIAIS DE SELECTION



CANCER DE L' OVAIRE

- Prévalence France 0.2 à 0.5 ‰
- Age moyen d'apparition 65 ans

  7 % survenue avant 40 ans

  10 % survenue entre 40 et 50 ans
- Malgré grandes cohortes trés faible nombre de cas
- degré de significativité non atteint
- Sous groupes faible importance

FACTEURS DE CONFUSION

Parité
Age a la première naissance
Prématurité
allaitement

Activité physique

Hystérectomie +/-
Salpingectomie uni /bi
Ovariectomie

CO durée

niveau socio économique

Origine ethnique

BMI ↗
Hormonothérapie substitutive

Grande taille

endométriose

CANCER OVAIRE

ATCD familiaux k ovaire

Mutation BRCA1 BRCA2

cancer colorectal héréditaire

Cancer sein ATCD personnel

tabagisme

HISTORIQUE cancer ovaire

AUGMENTATION significative du risque

- Whittemore 1992 526 £
  RR= 2.8 ttt RR= 27 ttt nulligeste
- Rossing 1994 3837 £
  RR= 11.1 si 12 cycles cc
- Brinton 2005 25152 £
- Källen 2011 19799 £
  OR=2.09 /pop. generale

PAS D AUGMENTATION SIGNIFICATIVE du risque

- Franceshi 1994
- Bristow 1996
- Mosgaard 1997
- Venn 1999 29700 £
- Ness 2002
- Lerner-Geva 2003 19146 £
- Jensen 2009 54362 £
- Van leeuwen 2002-2011 19146 £
- Brinton 2013 12193 £
- A-N Yli Kuha 2012 9175 £

INFERTILITE

- Neutraliser l'effet confusionnel de l'infertilité

Risque ajusté devient non significatif ?

- L'infertilité serait le facteur de risque sous jacent

Plutôt que l'effet des traitements ?

- Surveillance nécessaire au long cours

  Certaines sous population

human
reproduction
update

Controlled ovarian hyperstimulation for IVF: impact on ovarian, endometrial and cervical cancer—a systematic review and meta-analysis

Charalampos Siristatidis[1], Theodoros N. Sergentanis[2†], Prodromos Kanavidis[2†], Marialena Trivella[3,4], Marianthi Sotiraki[2], Ioannis Mavromatis[2], Theodora Psaltopoulou[2], Alkistis Skalkidou[5],

Synthèses de 9 COHORTES
109 969 femmes
76 cancers ovaire
1 seule étude > 10 ans

Table II Results of the meta-analyses examining the association between IVF and endometrial, ovarian and cervical cancer.

	Ovarian cancer				Endometrial cancer				Cervical cancer			
	n[a]	Effect estimate (95% CI)	P	Heterogeneity I^2, P[b]	n[a]	Effect estimate (95% CI)	P	Heterogeneity I^2, P[b]	n[a]	Effect estimate (95% CI)	P	Heterogeneity I^2, P[b]
Approach preferring[c] estimates which excluded the first year of follow-up after IVF												
Analysis versus general population	6	**1.50 (1.17–1.92)**	0.001	22.5%, 0.265	5	**2.04 (1.22–3.43)**	0.007	0.0%, 0.491	5	0.86 (0.49–1.49)[R]	0.585	70.2%, 0.009
Subanalysis on SIRs	4	1.19 (0.86–1.64)	0.293	0.0%, 0.679	3	**1.97 (1.15–3.40)**	0.014	33.8%, 0.221	3	1.54 (0.47–5.09)[R]	0.480	64.0%, 0.062
Subanalysis on ORs	2	**2.10 (1.43–3.10)**	<0.001	0.0%, 0.918	2	2.86 (0.52–15.75)	0.227	0.0%, 0.632	2	**0.60 (0.52–0.70)**	<0.001	0.0%, 0.661
Analysis versus infertile women[d]	2	1.26 (0.62–2.55)	0.521	0.0%, 0.451	2	0.45 (0.18–1.14)	0.093	0.0%, 0.789	1	5.70 (0.28–117.20)	0.259	NC, NC[e]
Approach preferring[c] estimates derived from total follow-up												
Analysis versus general population	6	**1.65 (1.07–2.55)[R]**	0.022	52.1%, 0.064	5	**1.97 (1.18–3.27)**	0.009	0.0%, 0.553	5	0.85 (0.49–1.48)[R]	0.556	70.8%, 0.008
Subanalysis on SIRs	4	1.42 (0.74–2.76)[R]	0.294	58.1%, 0.067	3	**1.97 (1.15–3.40)**	0.014	33.8%, 0.221	3	1.54 (0.47–5.08)[R]	0.480	63.9%, 0.063
Subanalysis on ORs	2	**2.13 (1.45–3.13)**	<0.001	0.0%, 0.769	2	1.91 (0.46–8.04)	0.376	0.0%, 0.923	2	**0.60 (0.52–0.70)**	<0.001	0.0%, 0.518
Analysis versus infertile women[d]	2	1.05 (0.55–2.01)	0.874	0.0%, 0.685	2	0.45 (0.18–1.14)	0.093	0.0%, 0.789	1	5.70 (0.28–117.20)	0.259	NC, NC[e]

Bold cells denote statistically significant associations. All pooled effect estimates were derived from fixed-effects analyses, except for cells marked with [R](random-effects).
CI, confidence interval. NC, not calculable.
[a]Number of studies.
[b]P-value derived from Cochran Q statistic.
[c]The distinction between the two follow-up intervals (excluding first year after IVF and total) was made only in three studies (Lerner-Geva *et al.*, 2003; van Leeuwen *et al.*, 2011; Yli-Kuha *et al.*, 2012).
[d]All analyses were based on IRRs.

ORIGINAL ARTICLE: ENVIRONMENT AND EPIDEMIOLOGY

In vitro fertilization and risk of breast and gynecologic cancers: a retrospective cohort study within the Israeli Maccabi Healthcare Services

Louise A. Brinton, Ph.D.,[a] Britton Trabert, Ph.D.,[a] Varda Shalev, M.D.,[b,c] Eitan Lunenfeld, M.D., M.H.A.,[b,c] Tal Sella, M.D.,[b,c] and Gabriel Chodick, Ph.D.[b,d]

2013 Fertility Sterility

TABLE 2

Adjusted hazard ratios for breast and gynecologic cancers associated with fertility treatments.

	Cases, n	Person-years	HR[a]	95% CI
Breast				
No fertility treatment	133	137,702	1.00	reference
Any fertility treatment	389	566,539	0.87	(0.71–1.06)
IVF	140	187,820	0.90	(0.71–1.15)
1–3 cycles	77	106,206	0.89	(0.67–1.18)
≥4 cycles	63	81,615	0.92	(0.68–1.24)
GnRH analogues	118	174,493	0.82	(0.64–1.05)
Clomiphene	284	426,797	0.87	(0.71–1.08)
Progestogen	278	450,928	0.80	(0.65–0.99)
Endometrial				
No fertility treatment	7	137,098	1.00	reference
Any fertility treatment	34	564,934	1.25	(0.55–2.84)
IVF	15	187,312	1.56	(0.63–3.86)
1–3 cycles	10	105,892	1.94	(0.73–5.12)
≥4 cycles	5	81,420	1.12	(0.35–3.56)
GnRH analogues	12	173,991	1.39	(0.54–3.55)
Clomiphene	20	425,861	1.01	(0.42–2.42)
Progestogen	27	449,807	1.24	(0.53–2.87)
Ovarian				
No fertility treatment	11	137,074	1.00	reference
Any fertility treatment	34	564,275	0.90	(0.45–1.79)
IVF	21	186,918	1.58	(0.75–3.29)
1–3 cycles	10	105,736	1.40	(0.59–3.32)
≥4 cycles	11	81,182	1.78	(0.76–4.13)
GnRH analogues	11	173,641	0.93	(0.40–2.16)
Clomiphene	20	425,227	0.75	(0.36–1.58)
Progestogen	23	449,283	0.77	(0.37–1.60)
Cervix in situ				
No fertility treatment	109	137,702	1.00	reference
Any fertility treatment	202	566,539	0.48	(0.38–0.61)
IVF	54	187,820	0.41	(0.29–0.56)
1–3 cycles	28	106,206	0.36	(0.24–0.54)
≥4 cycles	26	81,615	0.47	(0.31–0.72)
GnRH analogues	45	174,493	0.36	(0.25–0.50)
Clomiphene	140	426,797	0.44	(0.34–0.57)
Progestogen	142	450,928	0.42	(0.33–0.54)
Cervix invasive				
No fertility treatment	11	137,702	1.00	reference
Any fertility treatment	21	566,539	0.57	(0.27–1.19)
IVF	10	187,820	0.79	(0.34–1.88)
1–3 cycles	4	106,206	0.57	(0.18–1.79)
≥4 cycles	6	81,615	1.09	(0.40–2.96)
GnRH analogues	4	174,493	0.35	(0.53–2.87)
Clomiphene	12	426,797	0.45	(0.20–1.02)
Progestogen	10	450,928	0.34	(0.15–0.82)

Note: CI = confidence interval; HR = hazard ratio.

[a] Adjusted for age at entry, body mass index, smoking, parity at exit, and socioeconomic status; models included a term for the fertility treatment other than the type listed (e.g., for model of IVF treatment, model included term of IVF treatment and a term for other fertility treatment that was not IVF, so the reference was always no fertility treatment as listed).

Brinton. IVF and female cancers. Fertil Steril 2013.

87.403 femmes INFERTILES
Traitement 67608 34 cancers
Pas de traitement 19795 11 cancers
1994-2011
Suivi 8 ANS
45 cancers ovaire

AUCUN TTT D INFERTILITE NE POUVAIT ÊTRE RELIE A UN RISQUE SIGNIFICATIVEMENT AUGMENTE DE CANCER DE L OVAIRE

Mais augmentation si ≥ 4 cycles FIV
HR 1.40 95 % CI (0.59-3.32)
HR 1.78 (0.76-4.13)

2002

2011

human reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

Risk of borderline and invasive ovarian tumours after ovarian stimulation for *in vitro* fertilization in a large Dutch cohort

F.E. van Leeuwen[1,*], H. Klip[1,2], T.M. Mooij[1], A.M.G. van de Swaluw[1,3], C.B. Lambalk[4], M. Kortman[5], J.S.E. Laven[6], C.A.M. Jansen[7], F.M. Helmerhorst[8], B.J. Cohlen[9], W.N.P. Willemsen[10], J.M.J. Smeenk[11], A.H.M. Simons[12], F. van der Veen[13], J.L.H. Evers[14], P.A. van Dop[15], N.S. Macklon[6,16], and C.W. Burger[6]

Étude OMEGA

femmes infertiles 19.146 FIV / 6006 PAS DE FIV

1983 à 1995

moyenne de suivi 15 ans

nombreux paramètres étudiés

42 cancers ovaire 30 FIV / 12 NON FIV

Table II Incidence of ovarian malignancies by years of follow up and exposure status.

Follow-up	IVF group				Non-IVF group				Total			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
All ovarian malignancies												
<1 years	6	1.52	3.94	1.44–8.57	3	0.31	9.55	1.97–27.91	9	1.84	4.90	2.24–9.30
1–4 years	9	7.52	1.20	0.55–2.27	1	1.74	0.57	0.01–3.20	10	9.27	1.08	0.52–1.98
5–9 years	16	12.41	1.29	0.74–2.09	3	3.58	0.84	0.17–2.45	19	15.99	1.19	0.72–1.86
10–14 years	18	13.22	1.36	0.81–2.15	4	4.63	0.86	0.23–2.21	22	17.85	1.23	0.77–1.87
≥15 years	12	3.73	3.22	1.66–5.62	5	5.36	0.93	0.30–2.18	17	9.08	1.87	1.09–3.00
All intervals	61	38.41	1.59	1.21–2.04	16	15.63	1.02	0.59–1.66	77	54.03	1.43	1.12–1.78
All intervals excl. first year	55	36.88	1.49	1.12–1.94	13	15.31	0.85	0.45–1.45	68	52.20	1.30	1.01–1.65
Invasive ovarian cancer												
<1 years	2	0.78	2.57	0.31–9.26	3	0.16	18.35	3.79–53.60	5	0.94	5.30	1.72–12.37
1–4 years	5	3.94	1.27	0.41–2.96	1	0.93	1.07	0.03–5.97	6	4.88	1.23	0.45–2.68
5–9 years	4	6.90	0.58	0.16–1.48	2	2.03	0.99	0.12–3.56	6	8.93	0.67	0.25–1.46
10–14 years	10	8.13	1.23	0.59–2.26	2	2.85	0.70	0.09–2.54	12	10.98	1.09	0.56–1.91
≥15 years	9	2.54	3.54	1.62–6.72	4	3.68	1.09	0.30–2.79	13	6.22	2.09	1.11–3.57
All intervals	30	22.30	1.35	0.91–1.92	12	9.65	1.24	0.64–2.17	42	31.95	1.31	0.95–1.78
All intervals excl. first year	28	21.52	1.30	0.86–1.88	9	9.48	0.95	0.43–1.80	37	31.01	1.19	0.84–1.64
Borderline ovarian tumours												
<1 years	4	0.74	5.38	1.46–13.77	0	0.15	0	0.00–24.59	4	0.89	4.47	1.21–11.45
1–4 years	4	3.58	1.12	0.03–2.86	0	0.81	0	0.00–4.55	4	4.39	0.91	0.25–2.33
5–9 years	12	5.51	2.18	1.13–3.81	1	1.55	0.64	0.02–3.59	13	7.06•	1.84	0.98–3.15
10–14 years	8	5.09	1.57	0.68–3.10	2	1.79	1.12	0.14–4.04	10	6.87	1.45	0.70–2.68
≥15 years	3	1.18	2.53	0.52–7.40	1	1.68	0.60	0.02–3.32	4	2.86	1.40	0.38–3.58
All intervals	31	16.10	1.93	1.31–2.73	4	5.98	0.67	0.18–1.71	35	22.08	1.59	1.10–2.20
All intervals excl. first year	27	15.36	1.76	1.16–2.56	4	5.83	0.69	0.19–1.76	31	21.19	1.46	0.99–2.08

Obs, observed; Exp, expected; SIR, standardized incidence ratio; CI, confidence interval.

Cancer ovarien Van Leeuwen

- Pas d'augmentation significative FIV / NON FIV

SAUF AUGMENTATION SIGNIFICATIVE

APRES 15 ANS DE SUIVI

SIR=3.54 1.62-6.72 95% CI

(Persiste après ajustement parité et prise de co)

non retrouvé si pas de FIV

NULLIPARITE

Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

In vitro fertilization, endometriosis, nulliparity and ovarian cancer risk

Louise M. Stewart [a,*], C. D'Arcy J. Holman [a], Patrick Aboagye-Sarfo [a], Judith C. Finn [b,c], David B. Preen [a], Roger Hart [d,e]

2013

Suivi=16.7 ans

Table 1
Characteristics of the study population.[a]

Characteristic	All women in the cohort	Women undergoing infertility treatment but not IVF	Women undergoing IVF treatment
Number of women	21,646	14,098	7,548
Number of women who gave birth	14,907	10,032	4,875
Number of women diagnosed with ovarian cancer	38	22	16
Mean length of follow-up[b] (years)	16.9 ± 5.9	17.0 ± 5.9	16.7 ± 5.9
Total length of follow-up (years)	366,041	240,203	125,837
Mean age at start of follow-up (years)	31.2 ± 5.2	30.8 ± 5.3	32.1 ± 4.8
Mean age at first birth (years)	29.6 ± 6.0	28.3 ± 5.8	32.2 ± 5.4
Mean age at ovarian cancer diagnosis (years)	46.0 ± 7.0	46.7 ± 8.2	44.9 ± 4.8

Table 3
Multivariate regression models describing the relationship between ovarian cancer and identified risk and protective factors.[a]

Factor	Hazard ratio (95% CI) In the whole cohort (n = 21,646)	Hazard ratio (95% CI) In women who gave birth (n = 14,907)	Hazard ratio (95% CI) In women who did not have a recorded birth (n = 6,739)
Birth	0.49 (0.25–0.95)	-	-
IVF	1.36 (0.71–2.62)	1.01 (0.35–2.90)	1.76 (0.74–4.16)
Endometriosis	2.33 (1.02–5.35)	1.52 (0.34–6.75)	3.11 (1.13–8.57)

2011
1982-2006
1279 f FIV +cancer
Suivi=8 ans

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Malignancies among women who gave birth after *in vitro* fertilization

B. Källén [1,*], O. Finnström [2], A. Lindam [3], E. Nilsson [3], K.-G. Nygren [4], and P. Otterblad Olausson [3]

[1]Tornblad Institute, University of Lund, Biskopsgatan 7, SE-223 62 Lund, Sweden [2]Department of Paediatrics, University Hospital, SE-581 85 Linköping, Sweden [3]Department of Statistics, Monitoring and Analyses, Board of Health and Welfare, SE-106 30 Stockholm, Sweden [4]IVF and Fertility Clinic, Sophiahemmet, SE-114 86 Stockholm, Sweden

Table II Risk for cancer in women before they undergo IVF and women from the general population.

Cancer type	IVF women with cancer	All women with cancer	OR[a]	95% CI[a]
All cancers	747	19 799	1.37	1.27–1.48
Breast cancer	3	163	–	–
Cervical cancer, including cancer *in situ*	566	15 300	1.33	1.22–1.45
Ovarian cancer	29	296	3.93	2.63–5.64[b]
Placental cancer	15	900	0.83	0.50–1.38
CNS cancer	21	392	2.18	1.41–3.35
Malignant melanoma	36	853	1.18	0.85–1.66
Thyroid cancer	12	268	1.66	0.92–2.99
Colon cancer	6	204	1.36	0.50–2.97[b]
Other cancer	44	4796	1.10	0.81–1.50
All except ovarian cancer	718	19 503	1.33	1.24–1.44

Restricted to women who are parity 1 at their first pregnancy during the observation period.
[a]Odds ratio (OR) with 95% confidence interval (95% CI) after adjustment for year of delivery, maternal age at delivery and smoking. Number of women who underwent IVF = 18 643, the total number of women = 1 094 219.
[b]Relative risk (RR) calculated as observed over expected numbers, the latter estimated after adjustment as stated above.

Table III Risk for cancer in women after they have undergone IVF and other women who have an infant during the observation period.

Cancer type	IVF women with cancer	All women with cancer	OR[a]	95% CI[a]
All cancers	415	67 012	0.76	0.69–0.84
Breast cancer	91	13 583	0.76	0.62–0.94
Cervical cancer, including cancer *in situ*	164	33 538	0.61	0.52–0.71
Ovarian cancer	26	1779	2.09	1.39–3.12
Placental cancer	5	1236	0.28	0.12–0.64[b]
CNS cancer	17	1838	1.17	0.71–1.94
Malignant melanoma	37	3654	1.06	0.76–1.48
Thyroid cancer	10	943	1.16	0.55–2.13[b]
Colon cancer	11	1125	1.17	0.58–2.08[b]
Other cancer	54	9349	0.79	0.60–1.04
All except ovarian cancer	389	65 233	0.70	0.63–0.78

[a]Odds ratio (OR) with 95% confidence interval (95% CI) after adjustment for year of delivery, maternal age at delivery and smoking. Number of women who underwent IVF = 23 192, the total number of women = 1 365 179.
[b]Relative risk (RR) calculated as observed over expected numbers, the latter estimated after adjustment as stated above.

TUMEUR BORDERLINE OVAIRE

Augmentation significative risque

- Rossing 1994 RR 3.3
- Sushan 1996 RR=3.5
- Parrazini 2001 RR=27.5
- Ness 2002 RR=2.43
- Sanner 2009 RR =2.62
- Van Leeuwen 2011 RR=1.93
- Stewart 2013 RR=2.46

Pas d'augmentation de risque

- Mosgard 1997
- Yli- kuhna 2013

2002

2011

human reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

Risk of borderline and invasive ovarian tumours after ovarian stimulation for *in vitro* fertilization in a large Dutch cohort

F.E. van Leeuwen[1,*], H. Klip[1,2], T.M. Mooij[1], A.M.G. van de Swaluw[1,3], C.B. Lambalk[4], M. Kortman[5], J.S.E. Laven[6], C.A.M. Jansen[7], F.M. Helmerhorst[8], B.J. Cohlen[9], W.N.P. Willemsen[10], J.M.J. Smeenk[11], A.H.M. Simons[12], F. van der Veen[13], J.L.H. Evers[14], P.A. van Dop[15], N.S. Macklon[6,16], and C.W. Burger[6]

Étude OMEGA

femmes infertiles 19.146 FIV / 6006 PAS DE FIV

1983 à 1995

moyenne de suivi **15 ans**

nombreux parametres étudiés

35 tumeurs borderline ovaire 31 FIV / 4 NON FIV

TUMEUR BORDERLINE OVAIRE et FIV

Table II Incidence of ovarian malignancies by years of follow up and exposure status.

Follow-up	IVF group				Non-IVF group				Total			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
All ovarian malignancies												
<1 years	6	1.52	3.94	1.44–8.57	3	0.31	9.55	1.97–27.91	9	1.84	4.90	2.24–9.30
1–4 years	9	7.52	1.20	0.55–2.27	1	1.74	0.57	0.01–3.20	10	9.27	1.08	0.52–1.98
5–9 years	16	12.41	1.29	0.74–2.09	3	3.58	0.84	0.17–2.45	19	15.99	1.19	0.72–1.86
10–14 years	18	13.22	1.36	0.81–2.15	4	4.63	0.86	0.23–2.21	22	17.85	1.23	0.77–1.87
≥15 years	12	3.73	3.22	1.66–5.62	5	5.36	0.93	0.30–2.18	17	9.08	1.87	1.09–3.00
All intervals	61	38.41	1.59	1.21–2.04	16	15.63	1.02	0.59–1.66	77	54.03	1.43	1.12–1.78
All intervals excl. first year	55	36.88	1.49	1.12–1.94	13	15.31	0.85	0.45–1.45	68	52.20	1.30	1.01–1.65
Invasive ovarian cancer												
<1 years	2	0.78	2.57	0.31–9.26	3	0.16	18.35	3.79–53.60	5	0.94	5.30	1.72–12.37
1–4 years	5	3.94	1.27	0.41–2.96	1	0.93	1.07	0.03–5.97	6	4.88	1.23	0.45–2.68
5–9 years	4	6.90	0.58	0.16–1.48	2	2.03	0.99	0.12–3.56	6	8.93	0.67	0.25–1.46
10–14 years	10	8.13	1.23	0.59–2.26	2	2.85	0.70	0.09–2.54	12	10.98	1.09	0.56–1.91
≥15 years	9	2.54	3.54	1.62–6.72	4	3.68	1.09	0.30–2.79	13	6.22	2.09	1.11–3.57
All intervals	30	22.30	1.35	0.91–1.92	12	9.65	1.24	0.64–2.17	42	31.95	1.31	0.95–1.78
All intervals excl. first year	28	21.52	1.30	0.86–1.88	9	9.48	0.95	0.43–1.80	37	31.01	1.19	0.84–1.64
Borderline ovarian tumours												
<1 years	4	0.74	5.38	1.46–13.77	0	0.15	0	0.00–24.59	4	0.89	4.47	1.21–11.45
1–4 years	4	3.58	1.12	0.03–2.86	0	0.81	0	0.00–4.55	4	4.39	0.91	0.25–2.33
5–9 years	12	5.51	2.18	1.13–3.81	1	1.55	0.64	0.02–3.59	13	7.06•	1.84	0.98–3.15
10–14 years	8	5.09	1.57	0.68–3.10	2	1.79	1.12	0.14–4.04	10	6.87	1.45	0.70–2.68
≥15 years	3	1.18	2.53	0.52–7.40	1	1.68	0.60	0.02–3.32	4	2.86	1.40	0.38–3.58
All intervals	31	16.10	1.93	1.31–2.73	4	5.98	0.67	0.18–1.71	35	22.08	1.59	1.10–2.20
All intervals excl. first year	27	15.36	1.76	1.16–2.56	4	5.83	0.69	0.19–1.76	31	21.19	1.46	0.99–2.08

Obs, observed; Exp, expected; SIR, standardized incidence ratio; CI, confidence interval.

Van Leeuwen 2011 OMEGA

TUMEURS BORDERLINE OVAIRE et FIV

- Augmentation significative dans le groupe FIV/non fiv

- Surtout la première année SIR= 5.38 95 % CI 1.46- 13.77
  exclusion première année SIR= 1.76 1.16 - 2.56

- Population Pays-Bas
  0.45 % DEVIENDRAIT à 0.71 % a 50 ANS
  AVEC TTT FIV

- Pas de relation avec nombre de cycles ou type de traitement
  (Sous groupes faibles étude élargie en cours)

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In vitro fertilization is associated with an increased risk of borderline ovarian tumours

Louise M. Stewart [a,*], C D'Arcy J. Holman [a], Judith C. Finn [b,c], David B. Preen [a], Roger Hart [d,e]

2012

Table 2
Potential borderline ovarian tumour risk and protective factors.

Exposure	Number in exposed group	Crude (unadjusted) HR (95% CI)[a]	Adjusted HR (95% CI)[b]
IVF	7544	2.48 (1.22–5.04)	2.46 (1.20–5.04)
Birth[c]	14,902	0.70 (0.34–1.43)	0.89 (0.43–1.88)
Age at first birth			
No birth recorded	6737	1.00	1.00
Age<30 at first birth	7047	0.41 (0.15–1.13)	0.62 (0.20–1.87)
Age≥30 at first birth	7855	1.01 (0.46–2.21)	1.05 (0.48–2.34)
High socio-economic status[d]	5268	0.46 (0.16–1.30)	0.36 (0.12–1.03)
Diagnoses at baseline			
PID	3885	0.94 (0.36–2.45)	0.96 (0.37–2.51)
Endometriosis	2978	0.26 (0.04–1.92)	0.31 (0.04–2.29)
Procedures			
Sterilization	3740	1.55 (0.66–3.63)	1.48 (0.63–3.48)
Hysterectomy without USO[e]	2186	1.01 (0.24–4.34)	1.02 (0.24–4.37)

21639 Femmes
Australie
1982-2002
Suivi=16.9 ans
31 tumeurs borderline
14095 non fiv / 14 cas
7544 fiv / 17 cas
M DG = 8.6 années

Fertility drugs and the risk of breast cancer: a meta-analysis and review

Tony G. Zreik

Breast Cancer Res Treat (2010) 124:13–26

This meta-analysis of 23 carefully selected published case–controls (n = 8) and cohorts (n = 15) studies did not reveal an increased risk of breast cancer associated with the use of fertility drugs.

CANCER DU SEIN

RESEARCH www.AJOG.org

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

Breast cancer incidence after hormonal infertility treatment in Sweden: a cohort study

Chantal C. Orgéas, MPH; Karin Sanner, MD; Per Hall, MD, PhD; Peter Conner, MD, PhD; Jan Holte, MD, PhD; Staffan J. Nilsson, MD; Karin Sundfeldt, MD, PhD; Ingemar Persson, MD, PhD; Kee Seng Chia, MD, PhD; Sara Wedren, MD, PhD; Paul W. Dickman, PhD; Kamila Czene, PhD

2009
1135 femmes

TABLE 2
Characteristics of the study cohort comprising 1135 women attending 3 infertility clinics in Sweden between 1961 and 1976, with follow-up to Dec. 31, 2004, by breast cancer status

Characteristic	Women without breast cancer number (range)	Women with breast cancer number (range)
Total number of patients	1081	54
Total number of person-years of follow-up	35,092	1322
Median age at start of treatment (y) (IQR)	27 (6)	28 (6)
Median age at breast cancer diagnosis (y) (IQR)	—	53 (12)
Median time from start of treatment to breast cancer diagnosis (y) (IQR)	—	26 (10)

IQR, interquartile range.

Orgéas. Breast cancer incidence after hormonal infertility treatment. Am J Obstet Gynecol 2009.

TABLE 3
Standardized incidence ratios and 95% CI for breast cancer among women undergoing hormonal infertility treatment in Sweden between 1961 and 1976, for total follow-up period to Dec. 31, 2004, by exposure to hormonal treatment

Variable	Observed cases (n)	SIR (95% CI)[a]	SIR (95% CI)[b]
Any exposure to hormonal treatment	54	1.16 (0.89-1.52)	1.01 (0.77-1.31)
Type			
CC only	19	1.31 (0.83-2.05)	1.15 (0.73-1.80)
Gonadotropins only	9	0.63 (0.33-1.20)	0.53 (0.28-1.00)
Both (CC and gonadotropins)	26	1.48 (1.01-2.17)	1.28 (0.87-1.88)
Dose cycles (n)			
CC only, low (1-3)	7	0.91 (0.43-1.91)	0.80 (0.38-1.68)
CC only, high (4+)	12	2.15 (1.22-3.79)	1.90 (1.08-3.35)
Gonadotropins only, low (1-3)	4	0.58 (0.22-1.55)	0.49 (0.18-1.32)
Gonadotropins only, high (4+)	5	0.73 (0.30-1.76)	0.63 (0.26-1.51)

CC, clomiphene citrate; *CI*, confidence interval; *SIR*, standardized incidence ratios.

[a] Rates adjusted for attained age and calendar period of cancer diagnosis only. [b] Rates adjusted for attained age, calendar period of breast cancer diagnosis, total parity, and age at first term birth.

Orgéas. Breast cancer incidence after hormonal infertility treatment. Am J Obstet Gynecol 2009.

In vitro fertilization and breast cancer: is there cause for concern?

Louise M. Stewart, B.Sc.,[a] C. D'Arcy J. Holman, M.P.H., Ph.D.,[a] Roger Hart, M.D.,[b,e] Max K. Bulsara, Ph.D., M.Sc., B.Sc.,[d] David B. Preen, Ph.D.,[a] and Judith C. Finn, Ph.D., R.N.[c]

[a] School of Population Health; [b] School of Women's and Infants Health, and [c] Discipline of Emergency Medicine, The University of Western Australia, Crawley; [d] Institute of Health and Rehabilitation Research, University of Notre Dame, Fremantle; and [e] Fertility Specialists of Western Australia, Claremont, Western Australia, Australia

2012
21025 Femmes infertiles fiv/ ttt
M =17 ANS
1983- 2002

TABLE 2

Hazard ratios for breast cancer in women undergoing infertility treatment.[a]

Subgroup	Hazard ratio (95% CI)
IVF (no) (reference group)	1.00
IVF (yes)	1.10 (0.88–1.36)
Age <25 y at first delivery (reference group)	1.00
Age 25–29 y at first delivery	1.35 (0.86–2.13)
Age 30–34 y at first delivery	1.75 (1.13–2.72)
Age ≥35 y at first delivery	1.91 (1.20–3.03)
No birth recorded	1.16 (0.75–1.78)
No multiple birth (reference group)	1.00
Multiple birth	0.69 (0.41–1.16)

TABLE 3

Age-specific estimates of the effect of IVF on breast cancer rate.[a]

Age at start of infertility investigation (y)	Hazard ratio (95% CI) comparing breast cancer rate in women having IVF with women not having IVF: Unadjusted	Adjusted for confounding by age at first birth only	Adjusted for confounding by age at first birth and multiple delivery
20	1.86 (1.06–3.25)	1.69 (0.95–2.99)	1.80 (1.01–3.20)
24	1.59 (1.05–2.42)	1.47 (0.96–2.26)	1.56 (1.01–2.40)
28	1.36 (1.02–1.83)	1.29 (0.95–1.73)	1.34 (0.99–1.82)
32	1.17 (0.95–1.45)	1.12 (0.90–1.39)	1.16 (0.93–1.45)
36	1.00 (0.79–1.27)	0.98 (0.77–1.24)	1.00 (0.79–1.27)
40	0.86 (0.61–1.20)	0.85 (0.61–1.20)	0.87 (0.62–1.22)
44	0.74 (0.46–1.18)	0.74 (0.46–1.19)	0.75 (0.47–1.20)

[a] Estimates derived from Cox regression models that include the interaction between IVF and age at the specific ages shown. The first column of results shows the unadjusted analysis; the second gives hazard ratios after adjusting for confounding by age at first birth only; and the final model in the third column of results shows hazard ratios after adjusting for age at first birth and multiple birth.

Stewart. In vitro fertilization and breast cancer. Fertil Steril 2012.

Malignancies among women who gave birth after *in vitro* fertilization

B. Källén[1,*], O. Finnström[2], A. Lindam[3], E. Nilsson[3], K.-G. Nygren[4], and P. Otterblad Olausson[3]

[1]Tornblad Institute, University of Lund, Biskopsgatan 7, SE-223 62 Lund, Sweden [2]Department of Paediatrics, University Hospital, SE-581 85 Linköping, Sweden [3]Department of Statistics, Monitoring and Analyses, Board of Health and Welfare, SE-106 30 Stockholm, Sweden [4]IVF and Fertility Clinic, Sophiahemmet, SE-114 86 Stockholm, Sweden

*Correspondence address. Tel: +46-46-222-7536; Fax: +46-46-222-4226; E-mail: bengt.kallen@med.lu.se

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Table III Risk for cancer in women after they have undergone IVF and other women who have an infant during the observation period.

Cancer type	IVF women with cancer	All women with cancer	OR[a]	95 % CI[a]
All cancers	415	67 012	0.76	0.69–0.84
Breast cancer	91	13 583	0.76	0.62–0.94
Cervical cancer, including cancer *in situ*	164	33 538	0.61	0.52–0.71
Ovarian cancer	26	1779	2.09	1.39–3.12
Placental cancer	5	1236	0.28	0.12–0.64[b]
CNS cancer	17	1838	1.17	0.71–1.94
Malignant melanoma	37	3654	1.06	0.76–1.48
Thyroid cancer	10	943	1.16	0.55–2.13[b]
Colon cancer	11	1125	1.17	0.58–2.08[b]
Other cancer	54	9349	0.79	0.60–1.04
All except ovarian cancer	389	65 233	0.70	0.63–0.78

[a]Odds ratio (OR) with 95% confidence interval (95% CI) after adjustment for year of delivery, maternal age at delivery and smoking. Number of women who underwent IVF = 23 192, the total number of women = 1 365 179.
[b]Relative risk (RR) calculated as observed over expected numbers, the latter estimated after adjustment as stated above.

CANCER DU SEIN ET FIV

- Etude rassurante pour femmes débutant FIV a partir de 30 ans
- Surveillance accrue pour femmes entre 20 et 25 ans ?
- Connaitre ATCD familiaux

conclusions
represent a level 2a evidence, and a prospective study that can carefully capture all the relevant factors will help to generate a solid answer to this important question.

Conclusions

- Toute patiente candidate à une stimulation doit bénéficier d'un bilan gynécologique et sénologique complet.
- D'un interrogatoire sur ses ATCD personnels et familiaux.
- A ne pas négliger avec les années de suivi.

Conclusions

- Nous devons être concernés
- Par les risques de cancer chez nos patientes infertiles
- Par des risques surajoutés par la FIV
- A court terme
- A long terme
- Information nécessaire (nombre de tentatives ?)
- Obligation de succès / pas de cycles inutiles
- Registres , études et suivi indispensables .