Reproductive life events in the population living in the vicinity of a nuclear waste reprocessing plant.

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ABSTRACT

Objective: There is concern about the health of populations living close to nuclear waste reprocessing plants. We conducted a comparative study on reproductive life events in the general population living near the nuclear waste reprocessing plant in Beaumont-Hague, France and a reference area in Brittany.

Design, setting and participants: Women were randomly selected and retrospectively questioned on reproductive life events occurring between 1985 and 2000. Monthly probability of pregnancy (assessed by time to pregnancy, TTP, for pregnancy attempts leading or not to a live birth), occurrence of involuntary infertility, of spontaneous abortion and birth weight were compared between both areas using regression models with random effect.

Results: Compared to the reference area (326 couples) and after adjustment for sociodemographic and behavioural factors, couples from Beaumont-Hague (857 couples) had an estimated hazard ratio of pregnancy of 1.19 (95% confidence interval, 0.89 to 1.58). The prevalence ratio of 12-month involuntary infertility was 0.99 (95% confidence interval, 0.64 to 1.55) and the odds-ratio of spontaneous abortion was 0.86 (95% confidence interval, 0.85 to 1.33) for Beaumont-Hague, compared to the reference area. Mean birth weight was similar in both areas (95% CI of difference, -85 to 53 g).

Conclusion: We highlighted no increased risk of adverse reproductive life events in the population living in the vicinity of the French nuclear waste reprocessing plant, compared to the reference area. The reproductive health is unlikely to be strongly altered in the general population of Beaumont-Hague.

Concern about the health of the population living in the vicinity of nuclear waste reprocessing plants was raised by studies reporting an increased incidence of leukaemia in children living in Sellafield, around the Dounreay nuclear waste reprocessing plant (United Kingdom).[1] Similar studies around the French nuclear waste reprocessing plant in Beaumont-Hague, Normandy, also tended to show an increased risk of leukaemia in children.[2][3]

The reprocessing plant in Beaumont-Hague began operation in 1966. It has the capacity to process 1,650 tons of nuclear waste per year and has processed a total of about 15,000 tons of used nuclear fuel.[4] It releases radioactive compounds[5][6] and various chemicals (including dioxins and heavy metals[7]) into the air and sea. Moreover, a storage site for nuclear waste that has weak to average radioactive activity has been located in Beaumont-Hague since 1969. A nuclear plant operated by Electricité de France (EDF) is located a few kilometres away from Beaumont-Hague, in Flamanville and a military navy base that services nuclear submarines is located in Cherbourg (Figure 1).

Ionising radiation can influence semen quality,[8][9] which itself influences time to pregnancy.[10][11] Few studies directly assessed the association between male exposure to ionising radiation and a couple's fecundity,[12][13][14] all of which had limitations. One was limited by exposure misclassification[14]; another focused on primary infertility followed by a medical consultation,[13] which might not be a very sensitive marker of altered fecundity as not all couples choose to medicalize involuntary infertility; the third one concerned cancer patients,[12] among which confounding by indication cannot be discarded. Male occupational exposure to ionising radiation before conception of a pregnancy may influence the risk of stillbirth[15][16] and sex ratio.[17][18] An association between male radiodiagnostic X-rays before conception and birth weight of offspring was also reported.[19] Although oocytes are radiosensitive,[20] the possible effects of female exposure to ionising radiation on reproductive health are little documented.[12][21]

Male exposure to several chemical families is likely to influence fecundity, in particular inorganic lead,[22] solvents and some pesticides.[23] Male exposure to dioxin[24] and inorganic lead[25] has been related to the sex ratio of the offspring. Concerning female

exposures, heavy metals,[26] dioxin,[27] solvents,[26] may influence fecundity or birth outcomes.

The only studies that documented reproductive health in a population living around a nuclear waste reprocessing plant described the occurrence of stillbirth.[28][29][30] These studies reported no evidence of an increase in the risk of stillbirth with increasing proximity to Sellafield [28][30] nor at specific time periods with possibly higher exposure to radioactive compounds.[29] No study has documented fecundity and birth weight distribution in the general population living in the vicinity of nuclear waste reprocessing plants.

In this study, we compared the frequency of reproductive life events of the general population living in the vicinity of the nuclear waste reprocessing plant in Beaumont-Hague with that of a reference population.

MATERIALS AND METHODS

The 'canton' (electoral ward) of Beaumont-Hague is a rural area that had 10,900 inhabitants in 1999. The reference area was composed of four towns close to Saint-Brieuc, Brittany (Hillion, La Méaugon, Saint-Julien and Yffiniac, Figure 1), selected according to social class distribution and content of the subsoil in radionucleides (see appendix, WEB ONLY MATERIAL).

Population samples

We randomly selected private phone numbers among the subscribers of France Telecom in the study area. Each selected home was contacted by phone. In each home, a randomly selected woman aged between 18 and 60 years was eligible if it was her main residence and if she had been pregnant –regardless of the outcome - or had tried in the last 15 years (between January 1985 and April 2000) for one year or more to become pregnant. We proposed a refusal questionnaire to respondents who declined to participate. We recruited about twice as many homes in Beaumont-Hague than in the reference area. In each area, eligibility was defined irrespectively of occupational exposure to ionising radiation. The number of couples recruited in the reference area was chosen so as to allow a statistical power of 90% to detect a decrease by 1/3 in fecundability in Beaumont-Hague, compared to the reference area.[31]

Participation rate

We used data from the 1999 population census to estimate the participation rate. The census data did not contain information on the reproductive history of the women, but only on whether or not a child aged 15 years or less lived in the home. We used our data from the participating women to estimate the proportion of eligible women that had had a live birth in the last 15 years. We studied selection bias due to non-participation and to migration out of the study area (see appendix, WEB ONLY MATERIAL).

Questionnaires

Computer assisted telephone interviews were conducted between April and July, 2000. The 25 interviewers were trained for two days.

The woman was first asked to enumerate each of her pregnancies (including stillbirths, induced abortions and ectopic pregnancies) and attempts at pregnancy lasting at least 12 months. Next, the questionnaire focused on the previous 15 years (from January 1985): all pregnancies leading to a live birth, all spontaneous abortions (between 6 and 20 gestational weeks [32]) and pregnancies current at the time of the interview were detailed. The current male partner of the woman, if any, also answered a telephone questionnaire about his health, X-ray examinations [14] and occupation. The interviews were conducted simultaneously, by the same interviewers and with exactly the same methodology in both areas.

Fecundity

Time to pregnancy (TTP), the number of months between cessation of birth control and fertilization, was defined for live births for which the woman declared that neither partner was using any method to avoid pregnancy when pregnancy started. Values of zero and one month were grouped together.[33] TTP was not defined for pregnancies in couples who declared less than four sexual intercourses per month when they stopped using contraceptive methods. The women were asked if they had tried to become pregnant for at least one year between 1985 and 2000. They were then asked about the outcome of the pregnancy attempt as well as its duration and its date of termination. The exclusion of involuntarily infertile couples may lead to strong biases in the estimated impact of factors on fecundability.[22][34][35][36] Thus, we repeated the analyses defining also TTP for periods of involuntary infertility that started within the study period and that lasted at least one year without leading to any pregnancy.

Statistical analyses

The occurrence of reproductive health outcomes was compared between Beaumont-Hague and the reference area using regression models specified below and implemented with Stata SE 8.2 (Stata Corporation, College Station, TX) statistical package. All pregnancies or periods of unprotected intercourse among couples recruited in the study areas but who did not live yet in the area at the start of the pregnancy or pregnancy attempt were grouped into a third category ("other"). Unless otherwise specified, the statistical dependence between several pregnancies or pregnancy attempts of each woman was handled with random effect models.[37] In random effect models, only the intercept was assumed to be random, with a Gaussian distribution.

Adjustment factors:

Adjustment factors were *a priori* defined as the factors possibly associated with the considered health outcome (from the literature) and which were unlikely to be consequences of the health outcome or of the presence of the nuclear waste reprocessing plant. Coding of the quantitative adjustment factors was defined using non- and semiparametric approaches.[38]

TTP:

For the analysis of TTP and involuntary infertility, we restricted the analyses to periods of unprotected intercourse starting between January 1985 and July 1999, to limit the over-representation of long waiting times at the beginning of the study period and of short waiting times at the end of the study period.[39] TTP was censored at 13 months, or at the time of occurrence of a medical consultation for infertility, whatever came first. TTP was analysed with a discrete survival model with random effect, using a complementary log-log link.[37] The model estimates are expressed as monthly hazard ratios (HR) of pregnancy, a value smaller than one indicating a lower probability of pregnancy compared to the reference group. Tobacco smoking during the period of unprotected intercourse was taken into account as a time varying covariate.

Involuntary infertility:

We conducted two analyses with two different definitions of involuntary infertility. In both analyses, the referents were live births conceived less than 12 months after discontinuing birth control methods, for which the woman declared to have stopped using birth control methods in order to become pregnant and did not have a medical consultation for infertility during the period of unprotected intercourse. For the first analysis, a case was defined as a period of involuntary infertility lasting more than 12 months, regardless of the way the period ended (live birth, other pregnancy outcome, no pregnancy, cases A). For the second analysis, a case was defined as a 12-month period of involuntary infertility not leading to a live birth (cases B). Poisson regression with clustered variance estimates was used to estimate prevalence ratios of involuntary infertility.[40]

Spontaneous abortions:

The cumulative risk of spontaneous abortion from gestational weeks 6 to 20 was estimated using a survival approach.[32] Using logistic regression with random effect we compared pregnancies that lead to a spontaneous abortion with pregnancies that lead to a live birth.

Birth weight:

Linear regression with random effect was used to compare birth weight of singleton births between the two areas.

RESULTS

Study population

We contacted 2,503 homes with a respondent in Beaumont-Hague and 1,347 in the reference area; of these 3,850 homes, 1,183 included an eligible woman who participated (Figure 2). The participation rate, as estimated from the census data, was 75.6% in the Beaumont-Hague area and 67.2% in the reference area (overall participation rate, 73.0%). The comparison of the participating women with census data (WEB ONLY MATERIAL, Table S1) showed that we tended to under-represent women with little education, women with only one child, whereas those with three children tended to be over-represented. The mean number of children was similar to that expected from the census data.

Monthly probability of pregnancy

In Beaumont-Hague, 87.9% of the pregnancies started while the couple was not using a method to avoid pregnancy, compared to 90.7% in the reference area (WEB ONLY MATERIAL, Table S2; p=0.2). The hazard ratio (HR) of pregnancy comparing both areas was close to unity (Table 1; see also WEB ONLY MATERIAL Figure S1).

When the attempts at pregnancy not leading to a pregnancy were included, the adjusted HR of pregnancy in Beaumont-Hague changed very little (Table 1); the degree of significance associated with the age of the women decreased from p=0.34 to 0.05, and the adjusted HR of pregnancy associated with daily cigarette use exceeding 20 decreased (Table 1).

Involuntary infertility

The adjusted prevalence ratio of involuntary infertility in Beaumont-Hague, compared to the reference area, was close to unity whatever the definition of cases used (Table 2).

TABLE 1: Monthly hazard ratios (HR) of pregnancy and 95% confidence intervals (95% CI) in the Beaumont-Hague area, compared to the reference area. Unless otherwise specified, all variables are defined with respect to the start of the period of unprotected intercourse.

	Live births only (n=1444)				Live births and unsuccessful attempts at pregnancy (n=1517) *			
Characteristics	**n (%)**	**HR**	**95% CI**	**p**	**n (%)**	**HR**	**95% CI**	**p**
Raw models								
Area of residence								
Reference area	215 (15)	1			228 (15)	1		
Beaumont-Hague	611 (42)	1.01	0.77 to 1.32	0.96	641 (42)	1.07	0.81 to 1.41	0.65
Other †	618 (43)	0.93	0.71 to 1.20	0.57	648 (43)	0.99	0.75 to 1.29	0.91
Adjusted models								
Area of residence								
Reference area	206 (15)	1			218 (15)	1		
Beaumont-Hague	589 (43)	1.11	0.84 to 1.47	0.45	618 (43)	1.19	0.89 to 1.58	0.24
Other †	572 (42)	1.13	0.86 to 1.49	0.37	602 (42)	1.15	0.87 to 1.52	0.34
Woman's age (years)				0.34				0.05
<20	36 (3)	0.72	0.43 to 1.21		38 (3)	0.70	0.41 to 1.18	
20-24	459 (34)	0.86	0.71 to 1.03		472 (33)	0.90	0.75 to 1.09	
25-29	600 (44)	1			622 (43)	1		
30-34	222 (16)	0.98	0.78 to 1.23		241 (17)	0.87	0.69 to 1.10	
35-39	47 (3)	1.05	0.67 to 1.65		60 (4)	0.64	0.41 to 0.99	
≥ 40	3(0.2)	0.28	0.05 to 1.54		5 (0.4)	0.16	0.04 to 0.72	
Woman's body mass index ‡				0.70				0.36
<18 kg/m²	54 (4)	0.94	0.56 to 1.59		56 (4)	0.92	0.54 to 1.58	
18-29.9 kg/m²	1254 (92)	1			1315 (91)	1		
≥ 30 kg/m²	59 (4)	0.82	0.51 to 1.32		67 (5)	0.71	0.45 to 1.14	
Regularity of menstrual cycle				<0.01				<0.01
Regular	944 (69)	1			989 (69)	1		
Irregular	228 (17)	0.59	0.45 to 0.78		251 (17)	0.53	0.40 to 0.70	
Has always used hormonal contraception	195 (14)	1.16	0.87 to 1.54		198 (14)	1.29	0.96 to 1.73	
History of gynaecological disease §				<0.01				<0.01
No	1237 (90)	1			1295 (90)	1		
Yes	130 (10)	0.53	0.39, 0.74		143 (10)	0.53	0.38, 0.73	
Woman's tobacco consumption ¶				0.07#				0.05#
0	838 (61)	1			882 (61)	1		
1 - 10 cigarettes/day	316 (23)	1.01	0.81 to 1.26		337 (23)	0.90	0.72 to 1.13	
11 - 20 cigarettes/day	198 (14)	0.81	0.62 to 1.07		202 (14)	0.83	0.62 to 1.11	
> 20 cigarettes/day	15 (1)	0.58	0.25 to 1.37		17 (1)	0.38	0.15 to 0.95	
Year				<0.01				0.01
1985-1989	463 (34)	0.83	0.68 to 1.00		477 (33)	0.83	0.69 to 1.01	
1990-1994	518 (38)	1			542 (38)	1		
1995-1997	277 (20)	1.24	1.00 to 1.54		295 (21)	1.16	0.93 to 1.44	
1998-2000	109 (8)	1.68	1.23 to 2.31		124 (9)	1.40	1.02 to 1.91	

* Includes attempts at pregnancy lasting 12 months or more and not leading to a live birth or a spontaneous abortion.

† Category "other" corresponds to periods of unprotected intercourse among subjects recruited in either of the two areas but who did not live yet in the area of recruitment at the start of the considered period of unprotected intercourse.

‡ At interview.

§ Salpingitis, Chlamydia infection, cervical or uterine cancer, operation involving genital organs, endometriosis, ovarian cyst.

¶ Time-dependent variable taking into account a possible change in tobacco consumption during the period of unprotected intercourse.

Test for trend.

Spontaneous abortions

There was an 11.8% cumulative risk of spontaneous abortion for women in Beaumont-Hague and a 13.3% cumulative risk in the reference area. The adjusted odds-ratio (OR) of spontaneous abortion was 0.9 (Table 3) and changed little when a survival model was used (hazard ratio, 0.9, 95% CI 0.6 to 1.4), when the study period was restricted to 1990-2000 (OR=0.8, 95% CI, 0.5 to 1.4) or when only spontaneous abortions occurring after eight gestational weeks between 1990 and 2000 were considered (OR=1.1, 95% CI, 0.5 to 2.2).

Birth weight

There was no evidence of a decreased mean birth weight in Beaumont-Hague compared to the reference area (Table 4).

TABLE 2: Relative risks (RR) of involuntary infertility of one year or more in the Beaumont-Hague area, compared to the reference area. Poisson model with clustered bootstrap variance estimates. Unless otherwise specified, all variables are defined with respect to the start of the period of unprotected intercourse.

	Controls	Infertility cases									
	Live births with TTP<12 months * (n=1057)	A) All attempts >12 months (n=202)					B) Attempts>12 months not followed by a live birth (n=69)				
Characteristics	**n**	**n**	**(%) †**	**RR**	**95%CI**	**p**	**n**	**(%)‡**	**RR**	**95% CI**	**p**
Raw models											
Area of residence											
Reference area	156	26	(14)	1			9	(5)	1		
Beaumont-Hague	431	82	(16)	1.12	0.74 to 1.69	0.64	30	(7)	1.19	0.59 to 2.41	0.67
Other #	470	94	(17)	1.17	0.77 to 1.76	0.50	30	(6)	1.10	0.53 to 2.28	0.81
Adjusted models §											
Area of residence											
Reference area	151	24	(14)	1			9	(6)	1		
Beaumont-Hague	414	79	(16)	0.99	0.64 to 1.55	0.97	29	(7)	0.87	0.38 to 1.99	0.74
Other #	436	86	(16)	1.04	0.68 to 1.60	0.86	30	(6)	1.09	0.48 to 2.49	0.84
Woman's age (years)						0.02					<0.01
<25	346	74	(18)	1.29	0.91 to 1.82		15	(4)	0.91	0.49 to 1.72	
25-29	456	71	(13)	1			24	(5)	1		
30-34	165	26	(14)	0.99	0.66 to 1.50		14	(8)	1.45	0.71 to 2.96	
≥ 35	34	18	(35)	2.20	1.34 to 3.63		15	(31)	4.48	2.16 to 9.27	
Woman's body mass index ¶						0.05					0.05
<18 kg/m²	40	6	(13)	0.83	0.04 to 17.4		2	(5)	0.80	$2x10^{-5}$ to 3.10^{5}	
18-29.9 kg/m²	919	166	(15)	1			58	(6)	1		
≥ 30 kg/m²	42	17	(29)	1.79	1.11 to 2.88		8	(8)	2.25	1.17 to 4.32	
Regularity of menstrual cycle						<0.01					0.11
Regular	708	123	(15)	1			45	(6)	1		
Irregular	141	52	(27)	1.71	1.25 to 2.34		20	(12)	1.87	1.03 to 3.40	
Always used hormonal contraception	152	14	(8)	0.59	0.33 to 1.07		3	(2)	0.36	$4x10^{-4}$ to 291	
History of gynaecological disease **						<0.01					0.08
No	924	158	(15)	1			56	(6)	1		
Yes	77	31	(29)	1.82	1.23 to 2.70		12	(13)	1.85	0.94 to 3.62	

* Excludes couples who did not stop using a birth control method in order to become pregnant and those who had a medical consultation for infertility during the period of unprotected intercourse.

† Number of cases A / (number of cases A + controls).
‡ Number of cases B / (number of cases B + controls).
# Category "other" corresponds to periods of unprotected intercourse among subjects recruited in either of the two areas but who did not live yet in the area of recruitment at the start of the considered period of unprotected intercourse.
§ The model was adjusted for all variables in the table, year of the start of the pregnancy attempt and maternal smoking.
¶ At interview.
** Salpingitis, Chlamydia infection, cervical or uterine cancer, operation involving genital organs, endometriosis, ovarian cyst.

DISCUSSION

We highlighted no difference between the Beaumont-Hague area and the reference area for all reproductive life events considered. The pattern of the results was coherent across all studied events.

Reproductive health around nuclear waste reprocessing plants

In the Nord-Cotentin area, a risk assessment study based on the modeling of the dispersion of the discharges from the nuclear installations in the environment provided an estimate of the dose of ionising radiation to the bone marrow collectively received by subjects from the area until the age of 25 years. The bone marrow dose was considered unlikely to significantly contribute to the excess of leukaemia cases in children.[7] No estimate of the dose to the gonads was provided. The nuclear waste reprocessing plant also releases non radioactive chemicals (an incinerator was operated until 2002), in particular dioxins and heavy metals.[7] Male or female exposure to these compounds might influence reproductive health,[24][27][22][26] but few studies on the reproductive health of the population living near incinerators have been published.[41]

Former studies reported no increased risk of stillbirth with decreasing distance from a nuclear waste reprocessing plant.[28][29][30] Our study is the first to have focused on earlier foetal loss, fecundity and birth weight, which can more conveniently be studied in small geographical areas. Overall, these studies provide little evidence of alterations in reproductive health among the general population (taken as a whole) living around nuclear waste reprocessing plants. However, these studies, including ours, did not rely on individual estimates of exposure to radioactive or chemical discharges from the North-Cotentin nuclear installations.

TABLE 3: Odds-ratios (OR) of spontaneous abortion among 2,295 pregnancies (1999 live births and 296 spontaneous abortions) in the Beaumont-Hague area, compared to the reference area.

Characteristics	Number of pregnancies			OR	95% CI	p
	Total	Spontaneous abortions (%)				
Raw model						
Area of residence						
Reference area	324	47	(15)	1		
Beaumont-Hague	945	117	(12)	0.86	0.56 to 1.32	0.49
Other *	1026	132	(13)	0.92	0.61 to 1.40	0.70
Adjusted model †						
Area of residence						
Reference area	302	43	(14)	1		
Beaumont-Hague	899	108	(12)	0.86	0.55 to 1.33	0.49
Other *	898	100	(11)	0.87	0.55 to 1.37	0.55

* Category "other" corresponds to pregnancies among subjects recruited in either of the two areas but who did not live yet in the area of recruitment at the beginning of the considered pregnancy.
† The model was adjusted for female and male ages at conception (polynomial coding) , maternal height (<1.55 m, 1.55-1.70 and >1.70 m), weight (<50, 50-69, ≥ 70 kg), history of gynaecological disease, tobacco consumption (4 categories), alcohol consumption, year of conception (4 categories) and maternal socio-economic category.

Study population

In the absence of regional register on fecundity characteristics and on the relevant potential confounders, we selected a comparison area. The reference area was chosen because of its similarity to Beaumont-Hague in socio-economic characteristics, distance from the sea, and geological nature of the subsoil. This last criterion was meant to allow subsoil radioactivity (from natural origin) being similar in both areas. However, the fact that the concentrations in natural radionuclides of the subsoil were in the same range in both areas does not guarantee identical exposures of the population to subsoil ionising radiation of natural origin. Moreover, other environmental factors possibly influencing fecundity could differ between both areas. The mean number of children was similar between the included and the targeted population (WEB ONLY MATERIAL, Table S1), although women with one child were slightly under-represented in the study and women with three children or more were slightly over-represented. This pattern was however similar in both areas, so that this is in expectation unlikely to strongly bias our comparison. We could not include subjects who had lived in each area at some moment during the study period but who had moved away by the time the study was done. If, for instance, couples with involuntary infertility more often tended to move out than couples with a high fecundity, and if this happened more often in the Beaumont-Hague area, then a bias towards the null could be expected. Data from the 1999 population census indicated that in each area, among women aged 18 to 60 years in 1999, childless women living in the study area in 1990 were slightly more likely to move out of the area between 1990 and 1999 than women living in a home with at least one child aged up to 16 years in 1999. However, this trend was similar in both areas (WEB ONLY MATERIAL, Table S3). Although the number of children is probably a relatively poor marker of fecundity, this is not in favour of subfertile couples from Beaumont-Hague leaving more often the study area than subfertile couples from the reference area and hence not in favour of selection bias due to migration out of the study area.

Assessment of fecundity

The proportions of pregnancies that started while the couple was using a contraceptive method were similar in both areas. Imputing a TTP of one month to these pregnancies [14] and including them in the analysis yielded results similar to the main analysis (results not shown). Therefore, bias due to pregnancy planning is unlikely.

Reproductive life events were assessed by questionnaire with a recall period of up to 15 years. A study indicated that the quality of recall for TTP was satisfactory at the group level over a 15-year period for pregnancies that ended with live births.[42] Little is known about the quality of recall for periods of unprotected intercourse not leading to a live birth, which might be poor. However, excluding such events is likely to bias towards the null the estimated association between an exposure factor and fecundity.[22][36] The two separate analyses, one including and the other excluding unsuccessful attempts at pregnancy yielded similar conclusions for the comparison between Beaumont-Hague and the reference area. However, they yielded somewhat different results for other factors known to influence fecundity. For instance, the overall *p*-value associated with maternal age decreased when unsuccessful attempts at pregnancy were included, and the trend towards a decrease in the probability of pregnancy after 30 years became clearer. It had already been argued that pregnancy-based studies may bias the estimated effect of age on fecundity.[34][35] However, this had seldom been illustrated: Juul et al. reported a switch from negative age-dependence of fecundability in a European study including unsuccessful attempts at pregnancy to a lack of clear dependence when only women eventually pregnant were included,[35] whereas Joffe et al.[33] reported no strong change in the age effect on fecundability after inclusion of unsuccessful attempts at pregnancy among another European population.

In our study, the association between maternal smoking and probability of pregnancy tended to become stronger after inclusion of unsuccessful attempts at pregnancy. This can be seen as further empirical evidence that the exclusion of unsuccessful attempts at pregnancy can bias not only the estimated effect of age on fecundity, but also that of environmental factors

and that, in spite of possibly large recall errors on their occurrence, unsuccessful attempts at pregnancy should be included in retrospective TTP studies.[22][36]

To limit behaviour change bias, we asked women about changes in tobacco consumption during the period of unprotected intercourse, which allowed to code maternal tobacco use as a time-dependent variable in the survival model. Maternal tobacco use at the start of the period of unprotected intercourse was less clearly associated with the probability of pregnancy than this time-dependent variable: hazard ratios of pregnancy associated with a maternal smoking of 11-20 cigarettes/day and >20 cigarettes/day at the start of the period of unprotected intercourse were 1.05 (95% CI, 0.80 to 1.37) and 0.53 (0.22 to 1.24), respectively, compared to 0.83 and 0.38 for the same categories of the time-varying covariate (Table 3). Among the 12% of women who reported a change in tobacco use, about half reported that the change occurred during the first month of unprotected intercourse, and only 10% after month 4. Therefore, some women may change their tobacco consumption at the start or soon after the start of a pregnancy attempt, and, assuming that smoking has short term effects on fecundity, identifying these changes may be important to better characterize or control for the effect of tobacco use.

TABLE 4: Comparison of mean birth weight between the Beaumont-Hague area and the reference area, for 1965 singleton births delivered between 1985 and 2000.

Characteristics	n	%	Change in mean birth weight (g)	95% CI (g)	p
Raw model					
Area of residence					
Reference area	274	13.9	0		
Beaumont-Hague	820	41.7	-10	-86 to 66	0.80
Other *	871	44.3	-77	-150 to -5	0.04
Mean birth weight †	*1965*	*100*	*3440*	*3374 to 3506*	
Adjusted model ‡					
Area of residence					
Reference area	245	14.4	0		
Beaumont-Hague	737	43.4	-16	-85 to 53	0.65
Other *	717	42.2	4	-65 to 70	0.91
Gestational duration §					<0.01
Increase by 1 week	1699	100	18.3	16.4 to 20.1	
Maternal weight					<0.01
Increase by 10 kg, *below* 60kg §	675	39.7	116	53 to 179	
Increase by 10 kg, *above* 60kg §	1024	60.3	50	17 to 83	
Maternal height §					<0.01
Increase by 10 cm	1699	100	101	62 to 157	
Paternal height §					0.01
Increase by 10 cm	1699	100	51	12 to 90	
Gestational diabetes (mother)					0.11
No	1678	98.8	0		
Yes	21	1.2	154	-34 to 343	
Diabetes (father)					0.18
No or don't know	1687	99.3	0		
Yes	12	0.7	194	-91 to 479	
Woman's tobacco consumption					<0.01
0	1330	78.3	0		
1 to 4 cigarettes / day	118	6.9	-103	-170 to -36	
5 to 9 cigarettes / day	135	7.9	-164	-254 to -74	
≥10 cigarettes / day	116	6.8	-137	-279 to 5	
Environmental tobacco smoke					0.19
No	707	41.6	0		
Yes	992	58.4	-32	-80 to 16	
Mean birth weight (reference category) ¶	*1699*	*100*	*2645*	*1962 to 3329*	

* Category "other" corresponds to births among subjects recruited in either of the two areas but who did not live yet in the area of recruitment at the beginning of the considered pregnancy.

† Mean birth weight of babies born in the reference area.

‡ The model was adjusted for the sex of the newborn, year of conception and maternal alcohol consumption (above 7 glasses/week, continuous variable), parity (nulliparous, primiparous, multiparous) and all the variables listed in the table.

§ Continuous variable.

¶ Mean birth weight of babies with all covariate values corresponding to the reference categories, e.g. for a term female baby with a mother weighing 60 kg, 160 cm tall, nulliparous before the current pregnancy, with no diabetes, non-smoking, not drinking alcohol, with a male partner 175 cm tall.

Conclusions

Our study provides an assessment of several aspects of reproductive health events. We could control for most known potential confounders. Our estimates of the probability of pregnancy took into account periods of unprotected intercourse that did not lead to a pregnancy in less than 12 months, allowing for the inclusion of less fecund couples.[33] The main limitation of our study was the lack of individual information on exposure to radioactivity and chemical compounds, which is not easy to assess retrospectively because of the multiple pathways of exposure and the variety of compounds released. The retrospective design, also, does not allow discarding selection bias. Assuming an absence of such bias, the 95% confidence intervals of our estimates indicate that living in the vicinity of Beaumont-Hague nuclear waste reprocessing plant is unlikely to be associated with a decrease in the monthly probability of pregnancy greater than about 20%; it is unlikely to be associated with a risk of spontaneous abortion increased by more than one third, nor to be associated with a decrease in mean birth weight greater than 90 grams. Our study in the general population does not allow to draw conclusions on specific groups like those exposed to ionising radiation in an occupational setting or subjects exposed to the plants' discharges via specific behaviours. In conclusion, our study indicates that a strong increase of fecundity troubles, spontaneous abortion risk or a strong alteration of offspring birth weight in the general population living in the Beaumont-Hague ward during the 1985-2000 period is unlikely.

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COMPETING INTERESTS

None.

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What this paper adds?

What is already known on this subject?

-Possible increases in the risk of leukaemia in children have been reported around nuclear waste reprocessing plants in the United-Kingdom and France.

-The risk of stillbirth might be increased in relation with occupational exposure to ionising radiation, but probably not in the general population living around nuclear waste reprocessing plants.

What does this study add?

-The fecundity of the general population living around the French nuclear waste reprocessing plant is unlikely to be strongly altered. Similarly, a strong alteration of the birth weight distribution or of the risk of spontaneous abortion is unlikely.

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FIGURES

FIGURE 1: North-Western France. The study area is composed of the Beaumont-Hague ward (19 communes) and a group of 4 communes close to Saint-Brieuc (reference area, Hillion, La Méaugon, Saint-Julien and Yffiniac).

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FIGURE 2: Selection of the study population.

FIGURES

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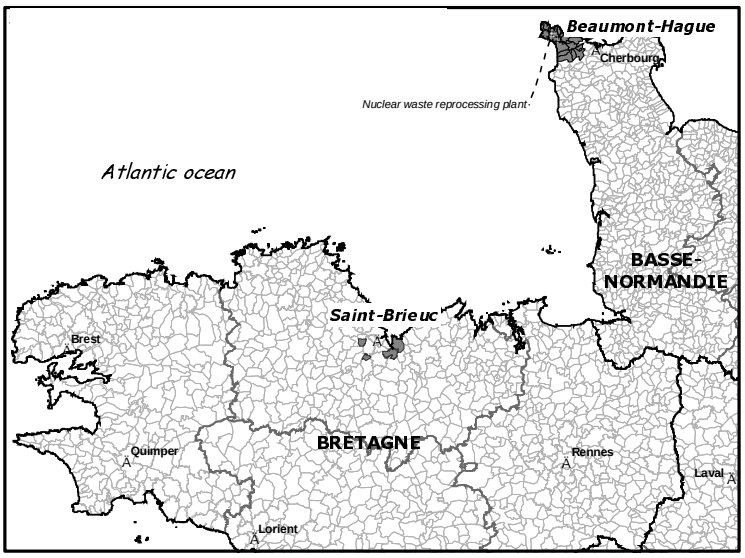
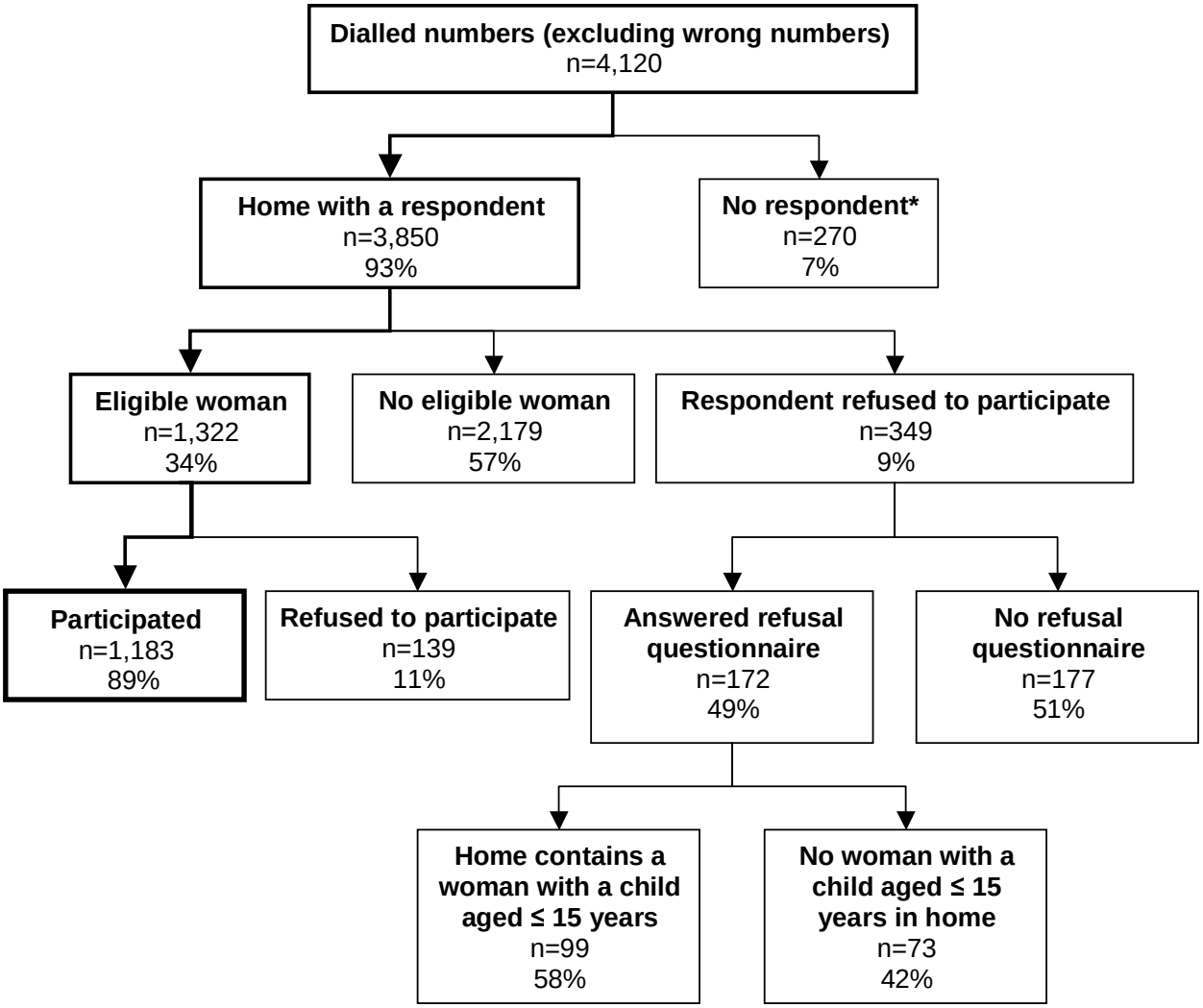


FIGURE 2: Flow chart of study population selection



* No reply after 15 calls on different days and at different times of the day.