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Infertility Treatment in France, 2008–2017: A Challenge of Growing Treatment Needs at Older Ages

Khaoula Ben Messaoud, MPH, Jean Bouyer, PhD, and Elise de La Rochebrochard, PhD

Objectives. To measure trends in infertility treatment use between 2008 and 2017 in France using data from the national health insurance system.

Methods. Between 2008 and 2017, we observed a representative national sample of nearly 1% of all women aged 20 to 49 years who were affiliated with the main health insurance scheme in France (more than 100 000 women observed each year). We exhaustively recorded all health care reimbursed to these women.

Results. Among women aged 20 to 49 years, 1.25% were treated for infertility each year. Logistic regression analysis showed a significant interaction between age and year of treatment use ($P < .001$). Over the decade, infertility treatment use increased by 23.9% among women aged 34 years or older, whereas among women younger than 34 years there was a nonsignificant variation.

Conclusions. Women aged 34 years or older were increasingly treated for infertility between 2008 and 2017.

Public Health Implications. Treatment efficiency decreases strongly with a woman's age, presenting a challenge for medical infertility care. (*Am J Public Health.* 2020;110: 1418–1420. doi:10.2105/AJPH.2020.305781)

The burden of infertility has been increasing since the 1990s worldwide and has had considerable public health consequences, including psychological distress, social stigmatization, economic strain, and marital discord.[1] In developed countries, the increase in infertility may be attributable to environmental exposure and social changes, including a major trend of delaying parenthood to an age interval marked by higher risk of infertility.[2,3]

In the United States, more than 1 in 10 women of reproductive age have ever used infertility services.[4] The Centers for Disease Control and Prevention have emphasized the need for the public health community to produce a more complete picture of infertility treatment use.[5] The lack of data is largely attributable to the exclusive focus of most research on the most complex infertility care (i.e., assisted reproductive techniques). Developing a surveillance system to guide authorities in elaborating plans for infertility prevention, detection, and management would be an important benchmark in measuring the global use of infertility treatments.[5]

In the United States, the use of infertility treatments is hindered by access barriers because of significant cost and lack of adequate health insurance among socially vulnerable people.[4,6] The global use of infertility treatments reflects both demand and access barriers. In France, 98% of residents (French and other nationalities) are covered by the health insurance system, which reimburses 100% of all infertility treatments. The French coverage of infertility treatment thus offers the opportunity to explore the global use of infertility treatment in a population-based approach and in a context of barrier-free financial access, although it has been shown that insurance coverage does not mean barrier-free access.[7]

Our objective was to assess the use of all infertility treatments in France between 2008 and 2017 using data from the French national health insurance database.

METHODS

In 2007, the French health insurance agency implemented a national sample including one ninety-seventh of the population covered by the main scheme (detailed presentation elsewhere[8]). Our study population was restricted to women aged 20 to 49 years.

We identified the list of infertility drugs using the Anatomical Therapeutic Chemical Classification System (Table A, available as a supplement to the online version of this article at http://www.ajph.org). We identified procedures related to assisted reproductive technology through the French classification system for medical acts (Classification *commune des actes médicaux*; Table B, available as a supplement to the online version of this article at http://www.ajph.org). For each year between 2008 and 2017, we classified a woman as having been treated for infertility during the year if she was reimbursed for at least 1 infertility drug or procedure. We measured the

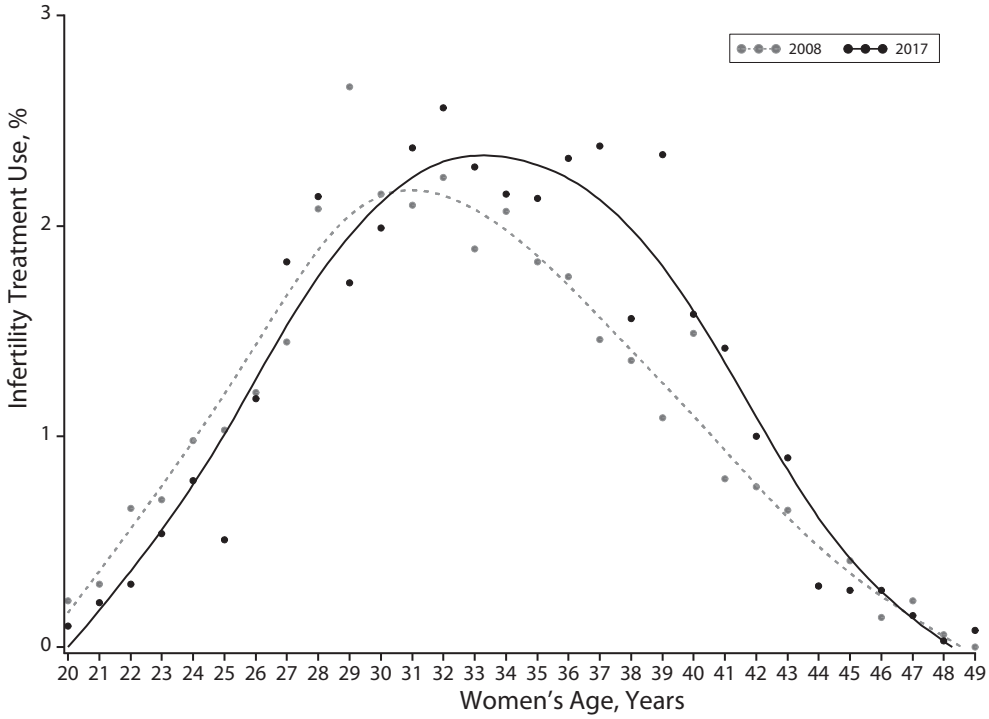
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Note. All infertility treatments are included (i.e., treatments with assisted reproductive technology [ART] and simple hormonal stimulation without ART). The figure shows women included in the one ninety-seventh sample of the French health insurance and affiliated with the main scheme. We used SAS INTERPOL = SM (for spline method) in PROC GPLOT (smoothing curve).

FIGURE 1—Infertility Treatment Use According to Women's Age: France, 2008–2017

use of infertility treatments as the number of women treated divided by the number of women aged 20 to 49 years.

We modeled the association between infertility treatment use and the woman's age using logistic regression. To test for a possible interaction with calendar year, we dichotomized age (threshold at 34 years) and included an interaction term with year. We carried out analyses using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Based on more than 100 000 women aged 20 to 49 years observed each year (Table C, available as a supplement to the online version of this article at http://www.ajph.org), 1.25% (95% confidence interval [CI] = 1.23, 1.27) of women were treated for infertility each year (detail by year in Figure A, available as a supplement to the online version of this article at http://www.ajph.org, and Table C).

The mean age of treated women was 33.0 years in 2008 and 33.7 years in 2017 ($P < .001$). In 2008 and 2017, infertility treatment use by age followed a bell curve with a shift toward older ages in 2017 (Figure 1).

In logistic regression analysis, interaction between age and year of infertility treatment use was statistically significant ($P < .001$; Figure B, available as a supplement to the online version of this article at http://www.ajph.org). Over the decade, infertility treatment use increased by 23.9% (95% CI = 14.66%, 33.74%; $P = .001$) among women aged 34 years or older, whereas, among women younger than 34 years, there was a nonsignificant variation of –5.00% (95% CI = –11.76%, 2.27%; $P = .170$).

DISCUSSION

Over the past decade in France, there has been a major increase in the use of infertility treatments among women aged 34 years and older but not among younger women.

In France, nearly all of the population (including non-French citizens) are fully covered for infertility treatments by the national health insurance scheme. This provides a unique opportunity to develop a strong and reliable population-based approach by considering all infertility treatments. However, potential limitations should be considered.

First, the study population included women covered by the main French health insurance scheme. This includes 76% of the total population and is considered a reliable source to study health in the French population.[9] Other schemes have been progressively added to the national sample between 2011 and 2016. We carried out sensitivity analysis including all French schemes for the year 2017 (Figure C, available as a supplement to the online version of this article at http://www.ajph.org). Results were reassuring, showing that the level of infertility treatment use and trend according to age was identical in our study population and in the population including all schemes.

Second, the French health insurance database does not include infertility treatment for French people who use cross-border reproductive care because of legal restrictions and an oocyte donation shortage in France.[10] These restrictions are likely to affect a limited number of people: specifically, women aged 43 years and older, same-sex couples, single people, women seeking oocyte donation, and people seeking surrogacy.

Third, we measured the use of hormonal stimulation treatments through information on treatment purchasing. It cannot be ruled out that a few women may have purchased the treatment but not used it, for example, because they became pregnant naturally before starting treatment.

Finally, the French health insurance database includes almost no data on the sociodemographic profile of the patients. For example, it would be interesting to explore the role of nulliparous status. However, this variable is not available, and we could not create it based on previous reimbursement for pregnancy or childbirth, as the database was too recent and did not include earlier reimbursements.

To the best of our knowledge, this is the first estimation of annual infertility treatment use in its entirety in a large population-based study. Estimates of global use of infertility treatments are mainly from the American National Survey of Family Growth, but they are lifetime estimates, and the size of the sample does not allow the exploration of annual estimates.[4] A small Spanish study of 443 women aged 30 to 49 years estimated the prevalence of infertility diagnosis at 1.26%.[11] This estimate is consistent with that observed in our study, but the outcome considered was different (infertility treatment use vs infertility diagnosis), and so was the age range of the population (20–49 years in our study vs 30–49 years in the Spanish study). One Canadian study explored change in treatment use over time according to age group and also observed increased use only among older women (30–44 years) and not among younger ones (20–29 years).[12] However, this study considered only treatment by clomiphene citrate.

PUBLIC HEALTH IMPLICATIONS

The increase in infertility treatment use among women aged 34 years and older is consistent with the social and demographic delay in parenthood until older ages that has been described since 1970 in high-income countries.[2] As the success rate of infertility treatments declines with women's age, health policymakers and clinicians should be aware of this time trend, as it could have an important impact on infertility medical care. By developing surveillance of infertility treatment use by age, the public health community could better guide national and international strategies to prevent and manage infertility, which emerges as a growing and major health issue among middle-aged people.[1,5] AJPH

CONTRIBUTORS

K. Ben Messaoud managed the data and performed the statistical analyses. K. Ben Messaoud and E. de La Rochebrochard have access to the data. J. Bouyer and E. de La Rochebrochard supervised the data management and statistical analyses. All authors conceptualized and designed the study, interpreted the data, drafted the brief, and read and approved the final version.

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CONFLICTS OF INTEREST

The authors declare no competing interests.

HUMAN PARTICIPANT PROTECTION

The study was reviewed and approved by the Institut national d'etudes démographiques ethics committee.

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Supplemental Table A. List[a] of Active Substances Used for Infertility Treatment, France, 2008-2017

Family	Anatomical therapeutic chemical class[a]	Active substance	Pharmaceutical product code[b]
Gonadotropins	G03G	Chorionic gonadotropin	3400930458075 3400930458426 3400930458594
	G03G	Human chorionic gonadotropin	3400927390920 3400935681614
	G03G	Urofollitropin	3400927435966 3400927436048 3400927436109 3400927436277 3400935777119 3400935777287 3400935777348 3400935777409 3400937609357 3400937609418 3400937609647 3400937609708
	G03G	Follitropin alpha	3400927903021 3400927903199 3400927903250 3400927939099 3400927939150 3400927939211 3400927939389 3400927939440 3400935779298 3400935779359 3400935779878 3400935780188 3400936347977 3400936348059 3400936348110 3400930089217 3400930089224 3400930089231
	G03G	Follitropin beta	3400934140969 3400935139931 3400935140012 3400935140241 3400935140302 3400935140531 3400935140760 3400935140999 3400935141071 3400935309747 3400935309808

Family	Anatomical therapeutic chemical class[a]	Active substance	Pharmaceutical product code[b]
Gonadotropins	G03G	Follitropin beta	3400936514133 3400935778987 3400935779588
	G03G	Lutropin alpha	3400935496430 3400935496669 3400921632033
	G03G	Choriogonadotropin alpha	3400921709476 3400935525796 3400936224520
Anti-estrogens	G03G	Clomifene citrate	3400932623389 3400932800988
GNRH agonists and antagonists	H01CA	Gonadorelin	3400932843633
	H01CA	Nafarelin	3400935352101
	H01CC	Ganirelix acetate	3400935530189 3400935530240 3400927517105 3400927517044
	H01CC	Cetrorelix acetate	3400935177902 3400935178152

[a] Infertility drugs were identified according to the Anatomical Therapeutic Chemical Classification classes (ATC). Three ATC classes were selected: gonadotropins and other ovulation stimulants (G03G), gonadotropin-releasing hormones (H01CA) and anti-gonadotropin-releasing hormones (H01CC). These three ATC classes include 12 active substances. Then, for each active substance, available drugs were identified by a pharmaceutical product code (Code Identifiant de Présentation, CIP). A total of 66 different drugs were identified.

[b] Pharmaceutical product code (Code Identifiant de Présentation, CIP)

Supplemental Table B. List of Medical Acts for Infertility Treatment, France, 2008-2017

Code[a]	Medical act for infertility
JJFC011	Oocyte retrieval by coelioscopy
JJFJ001	Transvaginal oocyte retrieval under ultrasound monitoring
JSEC001	Tubal embryo transfer by coelioscopy
JSED001	Transvaginal intrauterine embryo transfer
JSLD001	Intrauterine artificial insemination
JSLD002	Intracervical artificial insemination
YYYY032	Ovulation induction using gonadotropins followed by artificial insemination or in vitro fertilization

[a] Code of the French classification of medical acts (Classification Commune des Actes Médicaux, CCAM)

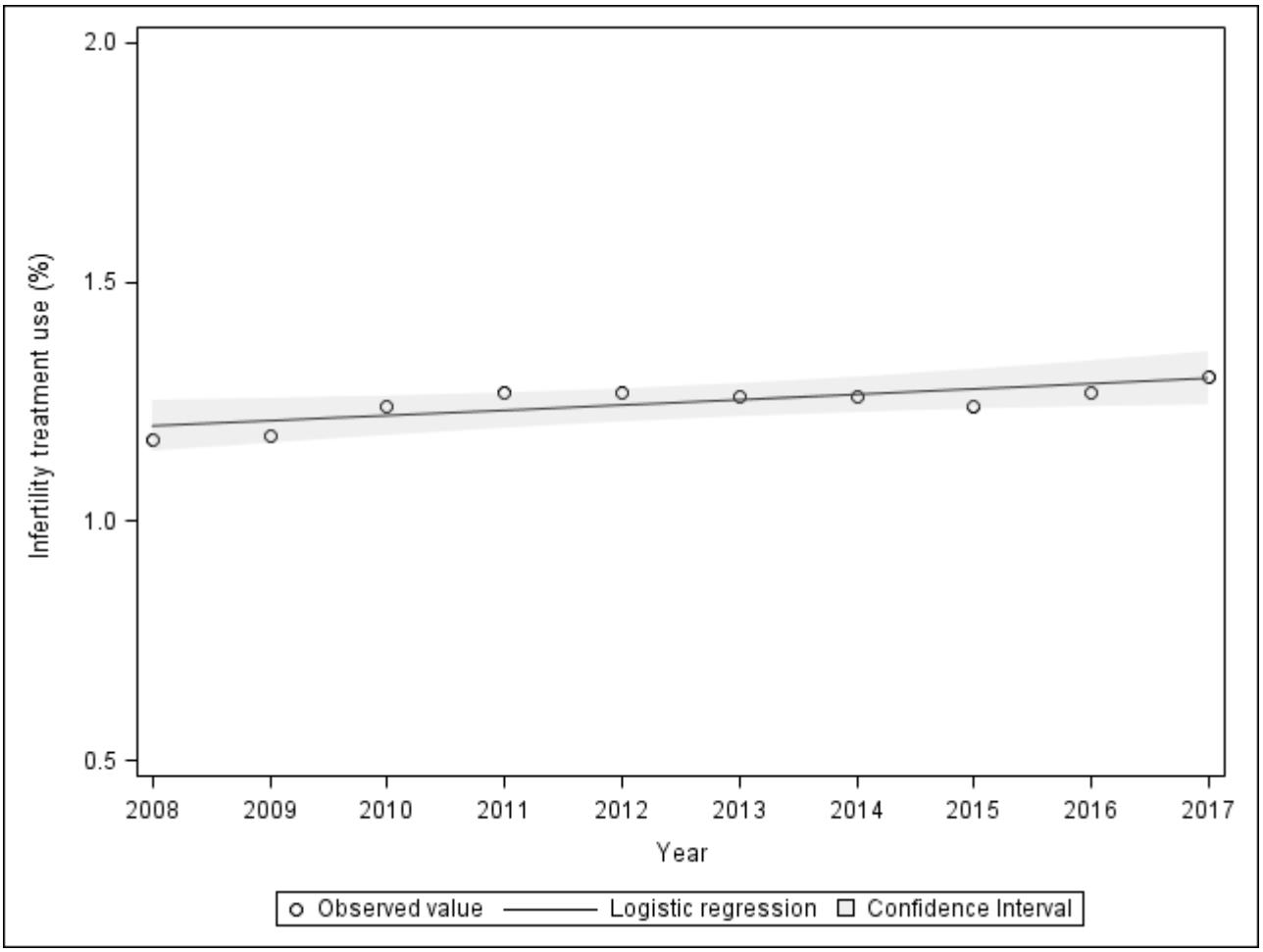
Supplemental Table C. Infertility Treatment[a] Use, France[b], 2008-2017

Year	Number of women aged 20-49	Number of women treated for infertility	Use of infertility treatments	
			%	95% confidence interval
Part A. Infertility Treatment Use among Women aged 20-49				
2008	105,521	1,233	1.17	[1.10; 1.23]
2009	105,596	1,248	1.18	[1.12; 1.25]
2010	108,909	1,350	1.24	[1.17; 1.31]
2011	107,847	1,367	1.27	[1.20; 1.33]
2012	108,864	1,384	1.27	[1.20; 1.34]
2013	109,085	1,378	1.26	[1.20; 1.33]
2014	109,170	1,380	1.26	[1.20; 1.33]
2015	109,460	1,355	1.24	[1.17; 1.30]
2016	109,733	1,399	1.27	[1.21; 1.34]
2017	110,942	1,446	1.30	[1.23; 1.37]
Part B. Infertility Treatment Use among Women aged 20-33				
2008	44,773	675	1.51	[1.39; 1.62]
2009	44,812	674	1.50	[1.39; 1.62]
2010	47,229	733	1.55	[1.44; 1.66]
2011	47,343	743	1.57	[1.46; 1.68]
2012	48,382	739	1.53	[1.42; 1.64]
2013	48,461	739	1.52	[1.42; 1.63]
2014	48,341	705	1.46	[1.35; 1.57]
2015	48,191	710	1.47	[1.37; 1.58]
2016	48,095	706	1.47	[1.36; 1.58]
2017	48,883	716	1.46	[1.36; 1.57]
Part C. Infertility Treatment Use among Women aged 34-49				
2008	60,748	558	0.92	[0.84; 0.99]
2009	60,784	574	0.94	[0.87; 1.02]
2010	61,680	617	1.00	[0.92; 1.08]
2011	60,504	624	1.03	[0.95; 1.11]
2012	60,482	645	1.07	[0.98; 1.15]
2013	60,624	639	1.05	[0.97; 1.14]
2014	60,829	675	1.11	[1.03; 1.19]
2015	61,269	645	1.05	[0.97; 1.13]
2016	61,638	693	1.12	[1.04; 1.21]
2017	62,059	730	1.18	[1.09; 1.26]

[a] All infertility treatments are included, i.e. treatments with assisted reproductive technology (ART) and simple hormonal stimulation without ART.

[b] Women included in the EGB (Echantillon Généraliste des Bénéficiaires) and affiliated to the main French health insurance scheme.

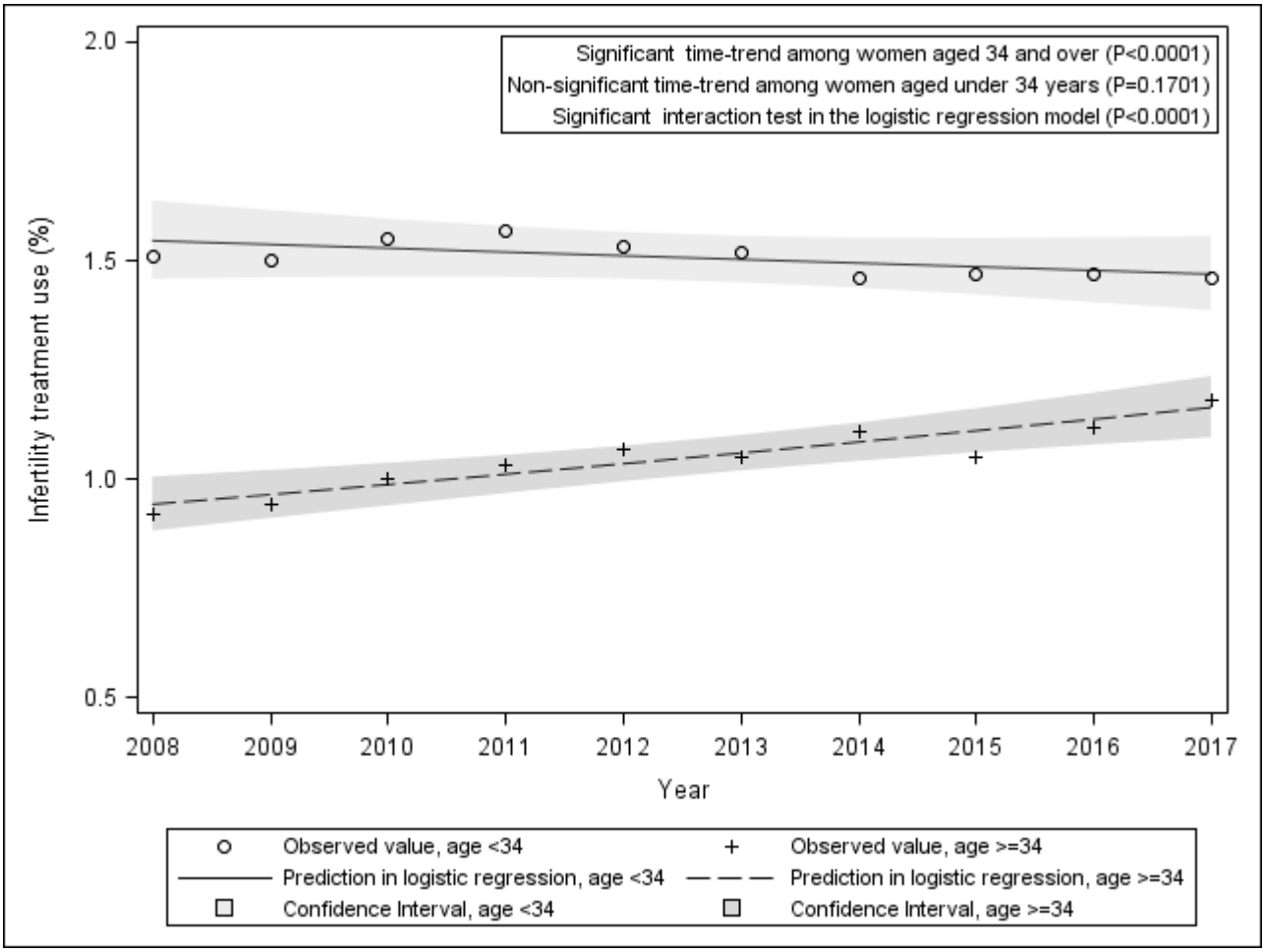
Supplemental Figure A. Infertility Treatment[a] Use among Women[b] aged 20-49, France, 2008-2017



[a] All infertility treatments are included, i.e. treatments with assisted reproductive technology (ART) and simple hormonal stimulation without ART

[b] Women included in the EGB (Echantillon Généraliste des Bénéficiaires) and affiliated to the main French health insurance scheme

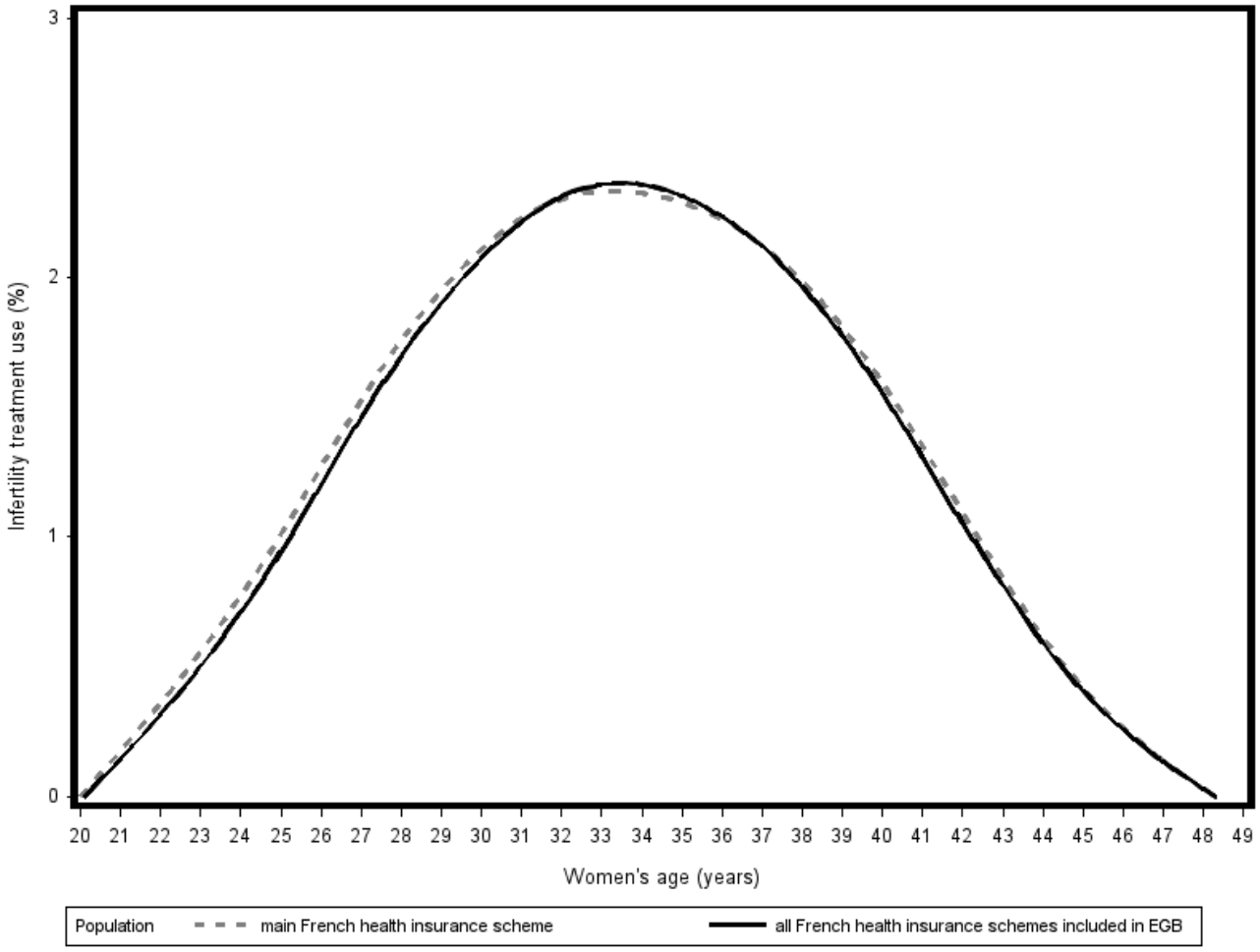
Supplemental Figure B. Logistic Regression Estimation of Infertility Treatment[a] Use among Women[b] aged ≥34 years and <34 Years, France, 2008-2017



[a] All infertility treatments are included, i.e. treatments with assisted reproductive technology (ART) and simple hormonal stimulation without ART

[b] Women included in the EGB (Echantillon Généraliste des Bénéficiaires) and affiliated to the main French health insurance scheme

Supplemental Figure C. Infertility Treatment[a] Use according to Women's Age, among Women[b] Covered by the Main French Health Insurance Scheme and by all Schemes, France, 2017.



[a] All infertility treatments are included, i.e. treatments with assisted reproductive technology (ART) and simple hormonal stimulation without ART.

[b] Women included in the EGB (Echantillon Généraliste des Bénéficiaires)