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No socio-economic differences in ART treatment success: Evidence from Careggi Hospital, Italy

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No socio-economic differences in ART treatment success: Evidence from Careggi Hospital, Italy

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Abstract

Objective. Several studies have shown stark socio-economic disparities in births born via assisted reproduction technology (ART), but only a few have investigated underlying causes. We study the likelihood of ART treatment success as a possible explanation.

Design. Observational study of center-based data. We consider women undergoing ART treatment at the ART-center in Careggi Hospital, Tuscany.

Outcome Measures. Probability of a conception following an ART treatment; probability of abortion after conception; and probability of a live birth after an ART treatment.

Results. The findings indicate no socio-economic disparity between patients with a high and low socio-economic status in the probability of achieving a successful ART treatment in terms of the probability of conception (β=0.02; 95% CI, -0.02, 0.06; P=0.362), abortion (β=-0.02; 95% CI, -0.08, 0.04; P=0.542) and live birth (β=0.02; 95% CI, -0.02, 0.06; P=0.291). The results also hold when focusing on patients at first treatment, only among natives, and by age groups.

Conclusions. Our findings suggest that within a public clinic providing subsidized access to treatments, socio-economic differences in the proportion of ART births may not stem from disparities in treatment success rates. Rather, other determinants relating to access to ART treatment such as geographical barriers, cultural preferences or knowledge about treatment success may play a larger role.

Keywords: ART; treatment success; social disparities

Capsule

We studied whether there are socio-economic differences in the likelihood of a successful ART treatment in terms of conception, abortion, and live birth. The findings reveal neither substantial nor significant differences.

Introduction

Since the first child was born via assisted reproduction technology (ART) in the late 1970s, ART has become a globally-used medical procedure (De Geyter et al., 2018). ART accounts for almost one-tenth of newborns in such countries as Spain and Denmark, and roughly three-to-four percent of newborns in countries as the United States, the United Kingdom, France, and Italy (Campo et al., 2023; Goisis et al., 2023; Scaravelli et al., 2024). Several phenomena have created these circumstances. For example, the postponement of parenthood at later ages (Beaujouan & Sobotka, 2022; Mills, Rindfuss, McDonald, & Te Velde, 2011; Tocchioni, Rybińska, Mynarska, Matysiak, & Vignoli, 2022) makes conception more difficult for new parents as their fecundity decays with age (Cito et al., 2019). Moreover, the increased diffusion and social acceptance of same-sex and single parents has also contributed to a larger pool of individuals relying on ART for their fertility desires (Raja, Russell, & Moravek, 2022). Overall, ART plays a pivotal role in granting reproductive rights and sustaining fertility desires, as well as in mitigating the fertility consequences of childbirth postponement on involuntary childlessness in high-income countries (Lazzari, Gray, & Chambers, 2021).

Despite the growing number of individuals resorting to ART to fulfill their fertility desires, the share of ART births is not equally distributed across socio-economic strata. Studies have consistently show substantial socio-economic gradients in the proportion of ART births across many high-income countries such as the United States, the United Kingdom, Denmark, Finland, Spain, France, and Italy with mothers from low socio-economic backgrounds systematically underrepresented (Campo et al., 2023; Goisis et al., 2023; Goisis, Håberg, Hanevik, Magnus, & Kravdal, 2020; Klemetti, Gissler, Sevón, & Hemminki, 2007; Wilcox & Mosher, 1993).

However, our understanding of underlying mechanisms remains limited. A possible mechanism is that women from low socio-economic backgrounds have a different rate of successful ART treatments. There may be at least two reasons behind this. First, women from lower socio-economic backgrounds may have, on average, poorer general health (Mackenbach et al., 2008), and may be more likely to engage in unhealthy behaviors

(Härkönen, Lindberg, Karlsson, Karlsson, & Scheinin, 2018; Pampel, Krueger, & Denney, 2010) – both of which can impact subfertility and, thus, their chances of a successful ART treatment (Rooney & Domar, 2014; Van Heertum & Rossi, 2017). Second, ART treatments are usually costly and time-consuming; consequently, women from lower socio-economic backgrounds can face more difficulties in complying with lengthy medical procedures or frequent commuting to reach treatment clinics (Lazzari, Baffour, & Chambers, 2022). Moreover, they may also have less medical knowledge and lower capabilities of following medical prescriptions and recommendations (Abel, 2008; Chang & Lauderdale, 2009). Therefore, they may have a smaller chance of treatment regimen adherence and, ultimately, success (Gameiro, Verhaak, Kremer, & Boivin, 2012).

In this article, we advance literature on socio-economic gradients in ART births by studying whether there are socio-economic differences in the probability of a successful ART treatment in terms of both conception and live birth, as well as abortion. We further investigate these disparities across population subgroups such as those at first treatment, native born, and by age groups. To this aim, we draw on the universe of ART treatments (N=4,747) performed at the ART-center in Careggi Hospital, Florence, Italy, between 2016 and 2021. Careggi is a public university hospital with an ART center in Florence, the regional capital of Tuscany, Italy. Nationally, it has been one of first centers to promote heterologous donor gametes ART treatments. Throughout the study period, the center offered ART treatments with heavy public subsidization. For instance, the out-of-pocket payment for the patient of a homologous intrauterine insemination amounted to 100 euros and an in vitro fertilization with oocyte donation to 500 euros (See Supplementary Table A1 for a full list of out-of-pocket payment costs, procedures costs fixed by the regional authority, and an explanation of the groups who can benefit of the out-of-pocket payment).

Materials and Methods

Data

We use data on ART treatments conducted at Careggi Hospital in Florence between 2016 and 2021. The data are of high quality as they had been collected directly by medical personnel overseeing the ART treatments and include socio-demographic, biometric, and treatment-related information pertaining to ART treatment and its potential success. The unit of analysis in the dataset is the ART treatment. There were 4,943 registered procedures conducted within the study period. From this number, we excluded only 3.97% of cases

(N=196) due certain information going unreported, such as the region or country of birth (N=31), marital status (N=145), and whether the treatment led to a conception (N=20). The final analytical sample consisted of N=4,747 treatments across N=2,709 patients.

Outcome variables

We have three binary outcome variables. The first outcome measures whether the ART treatment has led to a conception. In the period analyzed there has been a 34.59% conception rate. Conception is assessed by midwives and doctors following the patient at the ART-center. All women undergoing embryo transfer receive beta HCG dosage measurement after 15 days. In case of values above 30mUI/ml, the test is repeated after two days, and then an ultrasound scan is scheduled for 6-7 gestational weeks. The second outcome measures whether there has been a fetal loss, which is assessed via echography. This outcome is computed on the sub-sample of treatments leading to a conception. Spontaneous fetal loss happened to 24.61% of all conceptions. The third outcome is whether the treatment has led to a live birth. The live birth rate was 26.31%. For pregnancies carried out in other centers after the ART treatment, the personnel do trimestral phone calls to the patients until delivery. The medical personnel gather all delivery-related information, including birth outcomes.

Main predictor and its validation

The main predictor is a socio-economic status (SES) indicator of the patient, namely the self-reported occupational level transformed in the International Standard Classification of Occupations (ISCO) 2008, in 1 digit (Ganzeboom & Treiman, 1996). ISCO is a conventional, international, standard classification which categorizes occupations into 9 main hierarchical categories ranging from 1 referring to managers to 9 referring to unskilled workers. Medical personnel gather socio-demographic information of the patients when they begin treatment. We further operationalize the predictor by distinguishing between high-status occupations (ISCO 1 and 2) and medium/low status occupations (ISCO 3-9) – see Supplementary Table A2 for a detailed description of the ISCO groups and their coding. In the following, we refer to these two categories as the high and med/low SES. We also include two categories for women who were not employed at the time of the treatment and those who could not be classified. Among the 4,747 cases of ART treatments we observed: 16.85% were high SES, 34.93% med/low SES, 37.18% not employed, and 11.04% not classifiable (not shown in the main analyses but reported in the supplementary analyses).

To verify whether this variable captures socio-economic status, we test it on newborn's birth weight (BW). BW is a well-known heath indicator, and it is widely acknowledged that it is socially stratified (Cozzani, 2023; Kramer, Séguin, Lydon, & Goulet, 2000). We find BW to be stratified along our socio-economic indicator, with high SES having both heavier children and fewer low birth weight deliveries (<2.500 grams). Results are shown in Supplementary Figure A1. This finding proffers the validity of our SES marker based on women's occupations.

Control variables

In adjusted models, we include a large set of possible confounders, including: maternal age (continuous); the treatment order (first, second, third or more); whether the patient was attempting to transition to first parity; the treatment: intrauterine insemination (from partner or donor), intracytoplasmic sperm injection (ICSI), frozen embryo transfer (homologous or donor), in vitro fertilization (IVF); region of birth (or a residual category for those born abroad); and year of the treatment.

Methods

We estimate two sets of logistic regression models for ART conception, delivery, or abortion with and without adjustments, and compute and display predicted probabilities to allow for comparison across nested models in logistic regression (Mood, 2010; Norton & Dowd, 2018). Baseline models predict the probability of conceiving or delivering a child, or having an abortion, after an ART treatment only as a function of SES. Adjusted models include the set of covariates specified in the previous paragraph. Since data are at the treatment level and the same patient may have appeared more than once in the records due to multiple treatments, we cluster standard errors at the patient level.

Results

Descriptive results

Table 1 reports descriptive statistics for all patients and by patient SES. We observe very little difference in the probability of conception, abortion, and live birth across SES categories (i.e. high SES; med/low SES) and those who are not employed. The share of conceptions varies in a 2-percentage points range, between 33.7% for high SES and 35.8% for med/low SES. The probability of abortion is also comparable across the SES groups, with a 2.6 percentage point difference between high and med/low SES. Similarly, the probability of giving a live birth is also remarkably stable across SES groups: 25.2% for high SES and 27.5% for med/low SES. Moreover, we do not observe any other notable difference across SES groups for other characteristics, such as average maternal age at treatment, whether the treatment was aimed at conceiving the firstborn, the order of the treatment, and the number of embryos transferred. The only slight difference is that high SES are more likely to be born out-of-region.

[TABLE 1 ABOUT HERE]

Regression results

Figure 1 presents the predicted probabilities, represented as bars, along with their respective 95% confidence intervals (CIs), depicting the probability of successful conception and childbirth, or abortion following an ART treatment by maternal occupational status – high SES, med/low SES, and not employed. The blue dashed bars represent predicted probabilities derived from the baseline model, while the red bars denote those from the adjusted model (the full results are reported in Supplementary Table A3).

Overall, we do not observe any difference in the likelihood of conceiving, abortion, and delivering a child after ART treatment, both before and after adjustment for relevant confounders. In baseline models, we do not find any statistical difference ($P>0.05$) in the probability of conceiving a child after ART treatment (High SES: 33.7, 95% CI 30.34, 37.06; Med/low SES: 35.8, 95% CI 33.33, 38.27; Not employed: 33.6, 95% CI 31.2, 35.99), experiencing an abortion (High SES: 26.42, 95% CI 20.78, 32.05; Med/low SES: 23.87, 95% CI 20.16, 27.59; Not employed: 26.13, 95% CI 22.31, 29.96), or giving a live birth (High SES: 25.38, 95% CI 22.27, 28.48; Med/low SES: 27.68, 95% CI 25.03, 30.06; Not employed: 24.70, 95% CI 22.48, 26.93). We observe the same pattern of no statistically significant differences (P>0.05) in the probability of conceiving (High SES: 34.08, 95% CI 30.53, 37.64; Med/low SES: 36.08, 95% CI 33.54, 38.63; Not employed: 33.19, 95% CI 30.72, 35.65), abortion (High SES: 25.34, 95% CI 19.98, 30.69; Med/low SES: 23.32, 95% CI 19.59, 27.05; Not employed: 27.21, 95% CI 23.05, 31.38), or a live birth (High SES: 25.25, 95% CI 22.16, 28.34; Med/low SES: 27.53, 95% CI 25.16, 29.9; Not employed: 24.56, 95% CI 22.35, 26.78) after ART treatment in the adjusted models.

[FIGURE 1 ABOUT HERE]

Heterogeneity analyses

We further investigate whether the pattern of no SES differences remains if we focus instead on such subpopulations as those at first treatment, only Italian-born patients, and by age categories (≤35; 36-40; 40+). Figure 2 below displays 95% CIs adjusted predicted probabilities – excluding the indicator for which we split the analyses – of post-ART conception, abortion, and live birth.

The results presented in Figure 2 point toward the absence of socio-economic disparities. Among those at first treatment (upper panel), we do not observe any statistically significant difference (P>0.05) across SES groups regarding either the chance of conception (High SES: 30.2, 95% CI 25.93, 34.48; Med/low SES: 33.01, 95% CI 30.03, 35.99; Not employed: 32.91, 95% CI 29.77, 36.04), abortion (High SES: 28.34, 95% CI 20.61, 36.76; Med/low SES: 26.34, 95% CI 21.42. 31.27; Not employed: 27.74, 95% CI 22.38, 33.11), and live birth (High SES: 22.29, 95% CI 18.39, 26.19; Med/low SES: 24.45, 95% CI 21.74, 27.17; Not employed: 23.96, 95% CI 21.08, 26.83). Similar results are also obtained when we restrict the sample to only Italian-born patients (lower below) both in term of probability of conception (High SES: 34.48, 95% CI 30.74, 38.22; Med/low SES: 34.91, 95% CI 32.1, 37.72; Not employed: 35.62, 95% CI 32.54, 38.72), abortion (High SES: 26.88, 95% CI 21.01, 32.75; Med/low SES: 25.49, 95% CI 21.18. 29.80; Not employed: 26.45, 95% CI 21.80, 31.10), and live birth (High SES: 25.64, 95% CI 22.25, 29.02; Med/low SES: 26.06, 95% CI 23.37, 28.75; Not employed: 26.11, 95% CI 23.2, 29.02).

[FIGURE 2 ABOUT HERE]

We also replicate analyses on three age groups: women having 35 years old or less, women between 36 and 40, and women above 40. Figure 3 below displays the results by age group and outcome. Overall, we do not observe any disparity in any of the outcomes we considered.

[FIGURE 3 ABOUT HERE]

Sensitivity analyses

We perform two sensitivity analyses. First, as not all of the patients could be classified into a specific ISCO category, we also perform the above-described analyses for this category of patients. Results are reported in Supplementary Table A3. Also this category does not display any difference (P>0.05) with the other two SES groups and with those who were not employed. Second, we replicate our analyses using a more detailed version of SES distinguishing between medium (ISCO categories 3-5) and low (ISCO categories 6-9) groups (see supplementary Table A2 for a description of the coding). The results reported in supplementary Table A4 are fully consistent with the absence of a SES gradient in the likelihood of conception, abortion, and birth.

Discussion

Our study investigates whether there are any socio-economic disparities in ART treatment success in terms of the likelihood of conception and live birth using treatment data from the ART center in Careggi Hospital in Florence, Tuscany, Italy, between 2016 and 2021. The results show the absence of socio-economic differences in ART treatment success in terms of conception, live birth, or abortion, even after adjusting for important confounders.

These results have several implications for inequalities in ART-related births. First, we observed this result in a universalistic, heavily subsidized public center, where the cost of treatment is relatively affordable. The Tuscanian regional administration covers in fact most of the costs until the age 43 for homologous treatments, until age 43 for heterologous treatments involving sperm donation, and up to age 46 for heterologous treatments involving oocyte donation. Importantly, in Tuscany the access to ART is facilitated due to a clear regulation on procedures and access to public medical services. The access methods for homologous and heterologous assisted fertilization are defined in the Regional Council of Tuscany resolution 1197/2019 updated with the Council resolution 1121/2022. Moreover, in Tuscany, all pregnant women can rely on health equalization protocols. They are provided with a “pregnancy book”, in which they are scheduled for a minimum number of antenatal care visits, blood tests, and echo scans through the pregnancy. This could have contributed to guaranteeing higher attention and a better health status in this phase of life from all social strata. Further still, in Italy, pregnancy and delivery tend to be experienced with commitment, and with a certain amount of individual and social pressure, and are rarely seen as natural and physiological processes. Thus, the combination of affordable access and health equalization protocols may be important parameters when planning action to contrast inequalities in ART treatment success.

Second, this paper is particularly timely for Italy, given the planned – but yet to be implemented – introduction of the Essential Levels of Care for ART in 2024. The new rule will considerably reduce and standardize the cost of ART access for heterosexual couples throughout the country. At the time of writing, the cost of ART varies across regions, and the access of state-subsidized ART treatment is subject to age criteria. The impact of ART on Italian fertility is thus expected to grow as the new norms come into effect. Based on our findings, the new legislation has the potential to democratize the success of ART treatments across Italian regions.

Finally, it remains an open question which other factors may underly SES disparities in MAR births. In Italy, stark disparities in ART births were indeed noted: university-educated mothers are four times more likely to give birth via ART than mothers with a primary education; and slightly less than twice as likely than mothers with upper-secondary education (Campo et al., 2023). Since ART treatment success did not emerge as a possible explanation in SES disparities in ART access and birth in this study, other factors relating to access may play a role. For example, couples with a lower SES may also be more likely to live in more remote areas, which would increase their probability of having to commute longer distances to reach ART centers. Consequently, they may have higher constraints (e.g. time or capability of consistently attending visits) to access ART and initiate treatment (Lazzari et al., 2022). Moreover, compared to couples with a higher SES, a smaller proportion of couples with a lower SES could undergo ART treatments because of the minor effective needs of those treatments: childbearing postponement is more frequent among higher SES mothers (Baizan, 2020; Gottard, Mattei, & Vignoli, 2015) and, consequently, they are more prone to infecundity problems. Other possible reasons may include cultural attitudes towards the utilization of ART treatment, as well as in the understanding of treatment efficacy and risks (Präg & Mills, 2017). Overall, we suggest a larger emphasis on the attention placed on the distribution of ART centers across territories, as in the dissemination of correct knowledge on the conditions of treatment efficacy and success.

This study is not free from limitations. First, we focus on a single Center from Tuscany with high subsidization and therefore results should not be generalized to the whole universe of centers, as private clinics may have different outcomes. Nonetheless, our sample of patients is diverse, including almost half of the patients from all across the country. Second, our socio-economic indicator focused on capturing maternal occupational level, whereas most studies have focused on maternal education as main measure of SES. Nonetheless, occupation and education are usually highly correlated (Bernardi & Gil-Hernández, 2021; Ganzeboom, De Graaf, & Treiman, 1992).

However, this study also has considerable strengths. We were able to investigate all of the treatments with precise clinical and socio-economic information gathered by medical personnel over a time span of six years. We were also able to account for several potential confounders of the relationship between SES and ART treatment outcomes. Finally, our study is one of the few to specifically focus on the likelihood of ART treatment success in terms of both conception and live birth, as well as abortion, as a possible explanation for the disparities in MAR births observed in high-income countries.

Conclusions

Several studies have shown stark socio-economic differentials in ART births, but only a few have investigated underlying causes. We focused on the likelihood of an ART treatment's success in terms of both conception and live birth as a possible explanation. Our findings show no SES disparities in ART treatment success – a finding that holds for important sub-population groups.

Further research and policy attention should be focused on the determinants of access to fertility treatments, including barriers related to the distance to a clinic, and on such cultural factors as attitudes and knowledge toward treatment efficacy, success rate, and maternal and children's risks.

References

Abel, T. (2008). Cultural capital and social inequality in health. *Journal of Epidemiology and Community Health, 62*(7), e13-e13.

Baizan, P. (2020). Linking social class inequalities, labor market status, and fertility: An empirical investigation of second births. *Advances in Life Course Research, 46*, 100377.

Beaujouan, É., & Sobotka, T. (2022). Is 40 the new 30? Increasing reproductive intentions and fertility rates beyond age 40. *Optimizing the management of fertility in women over, 40*, 3-18.

Bernardi, F., & Gil-Hernández, C. J. (2021). The social-origins gap in labour market outcomes: compensatory and boosting advantages using a micro-class approach. *European Sociological Review, 37*(1), 32-48.

Campo, G., Boldrini, R., Di Cesare, M., Basili, F., Moroni, R., Romanelli, M., . . . Trevisani, V. (2023). G. Campo, R. Boldrini, M. Di Cesare, F. Basili, R. Moroni, M. Romanelli, E. Rizzuto, V. Trevisani. Certificato di assistenza al parto (CeDAP) 2022.

Chang, V. W., & Lauderdale, D. S. (2009). Fundamental Cause Theory, Technological Innovation, and Health Disparities: The Case of Cholesterol in the Era of Statins. *Journal of Health and Social Behavior, 50*(3), 245-260.

Cito, G., Coccia, M. E., Picone, R., Cocci, A., Russo, G. I., Garaffa, G., . . . Basile, V. (2019). Impact of advanced paternal age on the intracytoplasmic sperm injection (ICSI) outcomes in donor egg cycles. *Translational Andrology and Urology, 8*(Suppl 1), S22.

Cozzani, M. (2023). Inequalities at birth: stable socioeconomic differences in birth outcomes in three British cohorts. *Genus, 79*(1), 18.

De Geyter, C., Calhaz-Jorge, C., Kupka, M. S., Wyns, C., Mocanu, E., Motrenko, T., . . . Embryology. (2018). ART in Europe, 2014: results generated from European registries by ESHRE†: The European IVF-monitoring Consortium (EIM)‡ for the European Society of Human Reproduction and Embryology (ESHRE). *Human Reproduction, 33*(9), 1586-1601. doi:10.1093/humrep/dey242

Gameiro, S., Verhaak, C. M., Kremer, J. A. M., & Boivin, J. (2012). Why we should talk about compliance with assisted reproductive technologies (ART): a systematic review and meta-analysis of ART compliance rates. *Human reproduction update, 19*(2), 124-135. doi:10.1093/humupd/dms045

Ganzeboom, H. B., De Graaf, P. M., & Treiman, D. J. (1992). A standard international socio-economic index of occupational status. *Social Science Research, 21*(1), 1-56.

Ganzeboom, H. B., & Treiman, D. J. (1996). Internationally comparable measures of occupational status for the 1988 International Standard Classification of Occupations. *Social Science Research, 25*(3), 201-239.

Goisis, A., Fallesen, P., Seiz, M., Salazar, L., Eremenko, T., & Cozzani, M. (2023). *Educational gradients in the prevalence of Medically Assisted Reproduction (MAR) births in a comparative perspective*. (JRC132792).

Goisis, A., Håberg, S. E., Hanevik, H. I., Magnus, M. C., & Kravdal, Ø. (2020). The demographics of assisted reproductive technology births in a Nordic country. *Human Reproduction, 35*(6), 1441-1450.

Gottard, A., Mattei, A., & Vignoli, D. (2015). He Elationship Between Education and Fertility in the Presence of a Time Varying Frailty Component. *Journal of the Royal Statistical Society Series A: Statistics in Society, 178*(4), 863-881.

Härkönen, J., Lindberg, M., Karlsson, L., Karlsson, H., & Scheinin, N. M. (2018). Education is the strongest socioeconomic predictor of smoking in pregnancy. *Addiction*.

Klemetti, R., Gissler, M., Sevón, T., & Hemminki, E. (2007). Resource allocation of in vitro fertilization: a nationwide register-based cohort study. *BMC health services research, 7*(1), 1-8.
Kramer, M. S., Séguin, L., Lydon, J., & Goulet, L. (2000). Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? *Paediatric and Perinatal Epidemiology, 14*(3), 194-210.
Lazzari, E., Baffour, B., & Chambers, G. M. (2022). Residential proximity to a fertility clinic is independently associated with likelihood of women having ART and IUI treatment. *Human Reproduction, 37*(11), 2662-2671.
Lazzari, E., Gray, E., & Chambers, G. M. (2021). The contribution of assisted reproductive technology to fertility rates and parity transition. *Demographic research, 45*, 1081-1096.
Mackenbach, J. P., Stirbu, I., Roskam, A. J. R., Schaap, M. M., Menvielle, G., Leinsalu, M., . . . European Union Working Grp, S. (2008). Socioeconomic inequalities in health in 22 European countries. *New England Journal of Medicine, 358*(23), 2468-2481. doi:10.1056/NEJMsa0707519
Mills, M., Rindfuss, R. R., McDonald, P., & Te Velde, E. (2011). Why do people postpone parenthood? Reasons and social policy incentives. *Human reproduction update, 17*(6), 848-860.
Mood, C. (2010). Logistic regression: Why we cannot do what we think we can do, and what we can do about it. *European Sociological Review, 26*(1), 67-82.
Norton, E. C., & Dowd, B. E. (2018). Log Odds and the Interpretation of Logit Models. *Health Services Research, 53*(2), 859-878. doi:https://doi.org/10.1111/1475-6773.12712
Pampel, F. C., Krueger, P. M., & Denney, J. T. (2010). Socioeconomic disparities in health behaviors. *Annual Review of Sociology, 36*, 349.
Präg, P., & Mills, M. C. (2017). Cultural determinants influence assisted reproduction usage in Europe more than economic and demographic factors. *Human Reproduction, 32*(11), 2305-2314.
Raja, N. S., Russell, C. B., & Moravek, M. B. (2022). Assisted reproductive technology: considerations for the nonheterosexual population and single parents. *Fertility and Sterility, 118*(1), 47-53. doi:https://doi.org/10.1016/j.fertnstert.2022.04.012
Rooney, K. L., & Domar, A. D. (2014). The impact of lifestyle behaviors on infertility treatment outcome. *Current Opinion in Obstetrics and Gynecology, 26*(3), 181-185.
Scaravelli, G., Spoletini, R., Speziale, L., Fedele, F., Bolli, S., Mazzola, M., . . . Vigiliano, V. (2024). Medically assisted reproduction in Italy, 2020 data from the Italian MAR Register. *Minerva Obstetrics and Gynecology*.
Tocchioni, V., Rybińska, A., Mynarska, M., Matysiak, A., & Vignoli, D. (2022). Life-course trajectories of childless women: Country-specific or universal? *European Journal of Population, 38*(5), 1315-1332.
Van Heertum, K., & Rossi, B. (2017). Alcohol and fertility: how much is too much? *Fertility research and practice, 3*(1), 1-7.
Wilcox, L. S., & Mosher, W. D. (1993). Use of infertility services in the United States. *Obstetrics and Gynecology, 82*(1), 122-127.

Tables

Table 1. Descriptive statistics of ART treatments

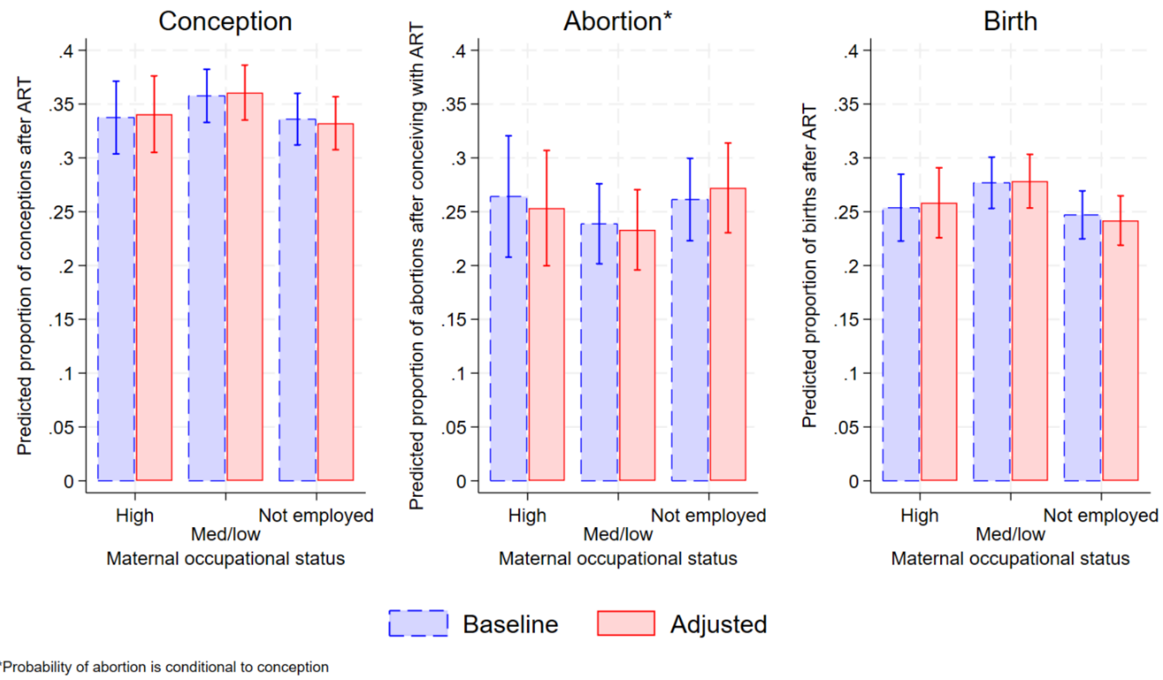
	Overall		High SES		Med/Low SES		Not employed	
	% value /Mean value	Std. dev.	% value /Mean value	Std. dev.	% value /Mean value	Std. dev.	% value /Mean value	Std. dev.
Outcomes								
Conception	34.59		33.71		35.80		33.60	
Abortion[a]	24.61		26.41		23.88		26.13	
Birth	26.31		25.24		27.53	.	24.57	
First birth	75.27		74.50		74.50		77.30	
Patient's age	38.25	4.85	38.57	4.49	38.33	4.53	38.15	5.29
Patient's marital status								
Cohabitation	37.62		39.62		43.61		31.05	
Married	62.10		60.25		55.91		68.78	
Single	0.27		0.12		0.48		0.17	
Patient's region of birth								
Tuscany	37.35		38.81		43.67		30.31	
Another region	40.85		51.12		36.29		41.58	
Foreign	21.80		10.07		20.04		28.11	
Treatment number								
First	56.98		55.47		58.73		57.07	
Second	27.45		27.99		26.99		27.15	
Third +	15.57		16.54		14.28		15.77	
Number of embryos transferred	1,46	0.64	1.37	0.62	1.45	0.32	1.52	0.17
N	4,747		800		1,658		1,765	

Note: descriptive statistics exclude ART treatments with not classifiable SES (N=524).

[a] Abortion percentage is computed on the sub-sample of those who conceived and have valid information on abortion (N=1,597).

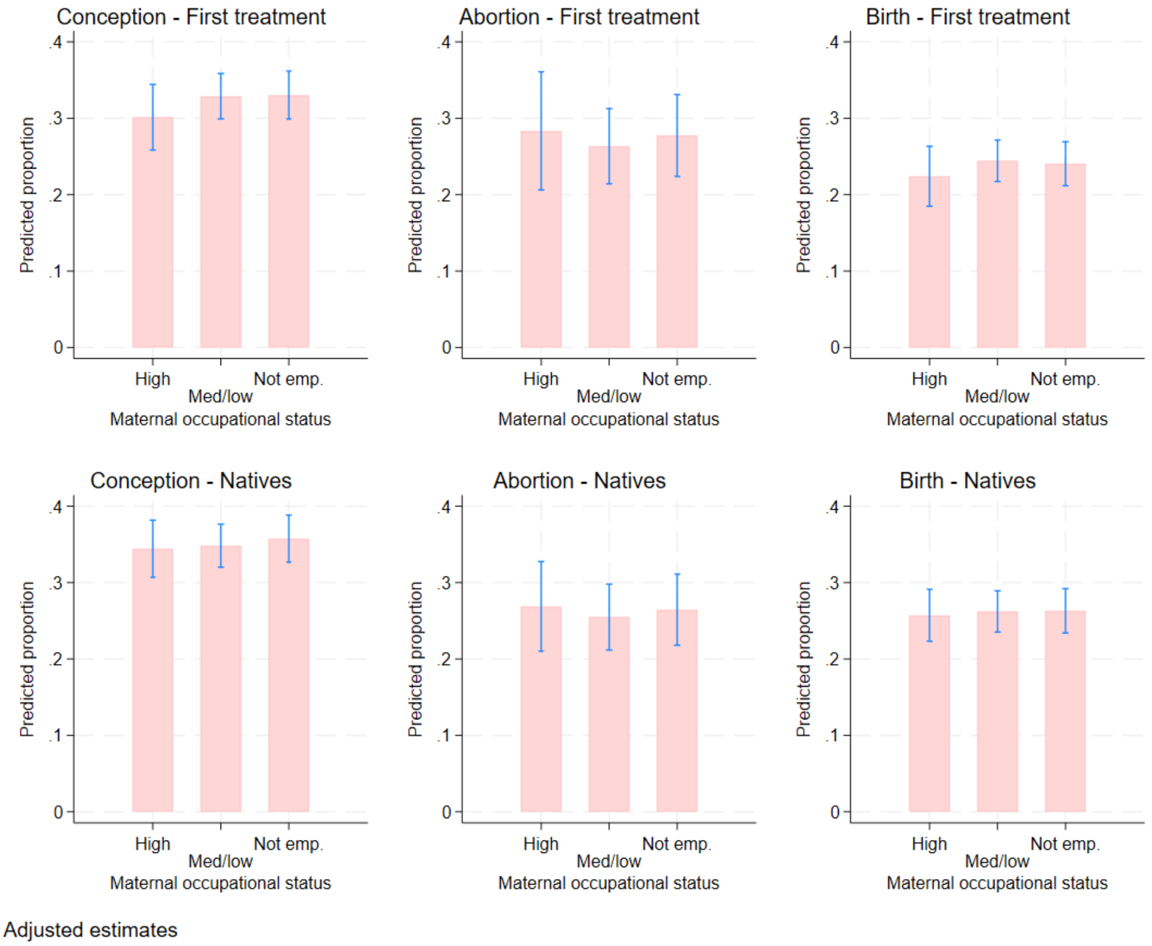
Figures

Figure 1. Predicted probabilities of conception (on the left), abortion (on the center), and birth (on the right) after ART by maternal occupational status. Careggi Hospital, Florence, Italy, 2016-2021



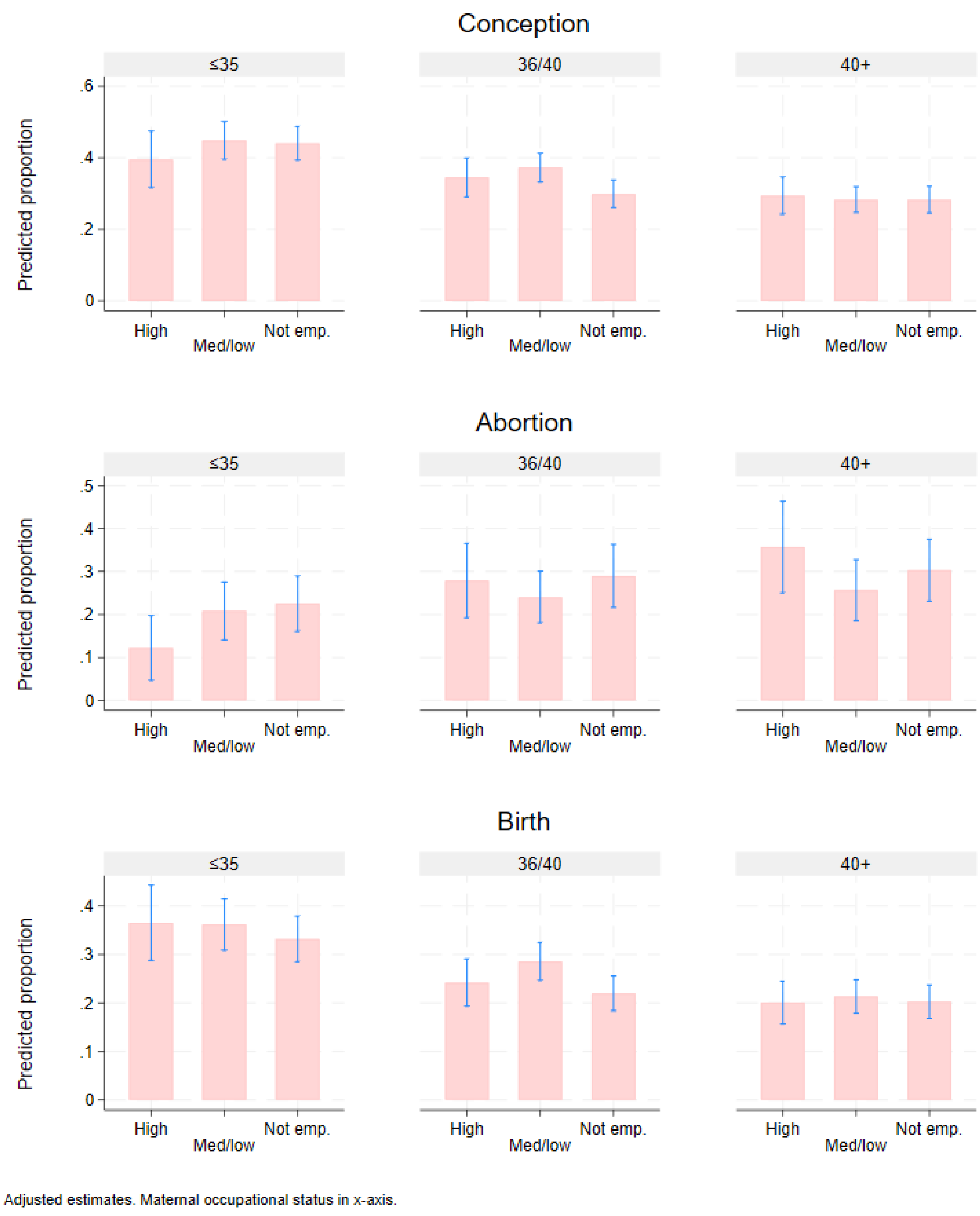
Note: predicted probabilities for baseline models obtained from a logit model including only the socio-economic indicator. Adjusted predicted probabilities are obtained from logit including controls for maternal age (continuous); treatment order; whether the patient is attempting to conceive the first child; kind of; whether treatment required third party semen; region of birth (or a residual category for those born abroad); year of the treatment.

Figure 2. Predicted probabilities of conception, abortion, and birth after ART by maternal occupational status, treatment order, and maternal nationality



Note: Adjusted predicted probabilities are obtained from logit including controls for maternal age (metric), nr of treatments (excluded in the upper panel); whether the patient is attempting to conceive the first child; kind of treatment; whether treatment required third party semen, region (or country in case of non-Italian patient) of birth (excluded in the bottom panel), and year of the treatment.

Figure 3. Predicted probabilities of conception and birth after ART by maternal occupational status and maternal age



Note: Adjusted predicted probabilities are obtained from logit including controls for nr of treatments; whether the patient is attempting to conceive the first child; kind of treatment; whether treatment required third party semen, region (or country in case of non-Italian patient) of birth, and year of the treatment.

Supplementary Materials

Tables

Table A1. ART treatment costs

(1)	(2)	(3)	(4)	(5)
Treatment	Out-of-pocket payment	Regional fixed cost	Regional fixed cost of male gamete donation from bank	Regional fixed cost of female gamete donation from bank
Homologous treatment	Euro	Euro	Euro	Euro
IUI	100.00	475.00		
IVF with or without Intracytoplasmic insemination (ICSI)	500.00	1,826.00		
IVF + ICSI + surgical sperm retrieval	500.00	2,549.00		
Heterologous treatments				
Intrauterine insemination (IUI) with male gametes donation	100.00	555.00	400	
In Vitro Fertilization (IVF) with male gametes donation	500.00	1,919.00	400	
IVF with oocyte donation	500.00	1,133.00		1,856

Note: The costs refer to the period considered in this analysis. Column (2) reports out-of-pocket payment for the patient. Column (3) reports the full cost of the procedure set by the regional council. Columns (4-5) report the cost of the of male and female gametes retrieval. For homologous treatments, out-of-pocket payments (instead of full cost) are available until age 43. For heterologous treatments, out-of-pocket costs are available until age 43 for semen donation procedures and until age 46 for oocyte donation procedures. After these age thresholds patients pay the full cost set by the Tuscany regional council.

Table A2. ISCO groups 1 digit and their classification

ISCO-08 groups 1 digit	SES definition main analyses	SES definition supplementary analysis
1. Managers	High	High
2. Professionals	High	High
3. Technicians and Associate Professionals	Med/low	Med
4. Clerical Support Workers	Med/low	Med
5. Service and Sales Workers	Med/low	Med
6. Skilled Agricultural, Forestry and Fishery Workers	Med/low	Low
7. Craft and Related Trades Workers	Med/low	Low
8. Plant and Machine Operators, and Assemblers	Med/low	Low
9. Elementary Occupations	Med/low	Low

Table A3. Average marginal effects (AMEs) from logistic models (Figure 1)

	(1)		(2)		(3)		(4)		(5)		(6)	
	Conception		Conception		Abortion		Abortion		Birth		Birth	
	AME	SE	AME	SE	AME	SE	AME	SE	AME	SE	AME	SE
Maternal SES												
High SES	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Med/Low SES	0.020	(0.021)	0.020	(0.022)	-0.025	(0.034)	-0.020	(0.033)	0.023	(0.020)	0.022	(0.021)
Not-employed	-0.002	(0.021)	-0.008	(0.023)	-0.003	(0.035)	0.019	(0.035)	-0.007	(0.019)	-0.015	(0.021)
Not class.	0.017	(0.029)	0.013	(0.028)	-0.070	(0.043)	-0.059	(0.042)	0.034	(0.027)	0.029	(0.027)
Marital Status												
Cohabiting			Ref.				Ref.				Ref.	
Single			-0.012	(0.179)			-0.040	(0.155)			0.055	(0.183)
Married			-0.009	(0.015)			-0.001	(0.024)			-0.010	(0.015)
Firstborn			-0.039*	(0.016)			-0.051*	(0.025)			-0.004	(0.016)
Age			-0.011***	(0.002)			0.006*	(0.003)			-0.010***	(0.002)
Nr. embryos.			0.120***	(0.014)			-0.018	(0.023)			0.106***	(0.013)
Technique Used												
IVF			Ref.				Ref.				Ref.	
IVF, ICSI			-0.046	(0.042)			0.087	(0.080)			-0.054	(0.039)
ICSI			-0.067*	(0.027)			0.032	(0.044)			-0.051*	(0.025)
IUI - hom.			0.174*	(0.073)			0.052	(0.112)			0.168*	(0.072)
IUI het.			-0.060	(0.055)			-0.134	(0.079)			0.004	(0.054)
FET			0.055*	(0.027)			-0.025	(0.043)			0.054*	(0.025)
First Treat.			0.000	(.)			0.000	(.)			0.000	(.)
Second			0.047**	(0.015)			-0.046*	(0.023)			0.048***	(0.014)
Third +			0.029	(0.021)			-0.023	(0.032)			0.027	(0.020)
Region of birth												
Abruzzo			Ref.				Ref.				Ref.	
Basilicata			-0.053	(0.086)			-0.143	(0.122)			-0.005	(0.088)
Calabria			-0.070	(0.078)			0.067	(0.113)			-0.074	(0.073)
Campania			-0.065	(0.070)			-0.086	(0.100)			-0.027	(0.069)
Emilia-Romagna			-0.083	(0.079)			-0.058	(0.114)			-0.053	(0.078)
Friuli-Venezia Giulia			-0.221	(0.250)			0.000	(.)			0.000	(.)
Lazio			-0.136	(0.071)			-0.090	(0.103)			-0.075	(0.069)
Liguria			-0.149	(0.092)			-0.184	(0.124)			-0.057	(0.091)
Lombardia			-0.062	(0.076)			-0.007	(0.112)			-0.018	(0.074)
Marche			-0.228*	(0.091)			-0.064	(0.153)			-0.156	(0.086)
Molise			-0.174	(0.113)			0.078	(0.199)			-0.160	(0.083)
Piemonte			-0.132	(0.080)			-0.009	(0.123)			-0.101	(0.075)
Puglia			-0.044	(0.080)			-0.120	(0.106)			0.003	(0.078)
Sardegna			-0.212*	(0.089)			-0.109	(0.138)			-0.151	(0.083)
Sicilia			-0.021	(0.075)			-0.083	(0.108)			0.006	(0.075)
Toscana			-0.084	(0.066)			-0.046	(0.095)			-0.046	(0.065)
Trentino Alto Adige			-0.131	(0.337)			0.000	(.)			0.017	(0.337)
Umbria			-0.186*	(0.092)			-0.098	(0.138)			-0.126	(0.087)
Veneto			-0.066	(0.090)			-0.126	(0.123)			0.016	(0.086)
Foreign born			-0.124	(0.067)			-0.083	(0.096)			-0.065	(0.066)
Year of birth												
2016 (Ref.)			Ref.				Ref.				Ref.	
2017			0.040	(0.026)			0.078	(0.040)			0.000	(0.026)
2018			0.055*	(0.028)			0.058	(0.042)			0.027	(0.026)
2019			0.013	(0.028)			0.045	(0.043)			0.005	(0.027)
2020			-0.007	(0.029)			0.072	(0.047)			-0.017	(0.028)
2021			0.045	(0.029)			0.019	(0.044)			0.047	(0.029)
N	4,747		4,747		1,597		1,595[b]		4,747		4,743[a]	

Note: AME are obtained from logistic models. Columns (1, 3, 5) report baseline models; columns (2, 4, 6) report adjusted models. [a] We lose four cases for collinearity between Friuli Venezia Giulia and control variables. [b] We lose two cases for collinearity between region of birth (Friuli Venezia Giulia, Trentino AA) and other control variables.

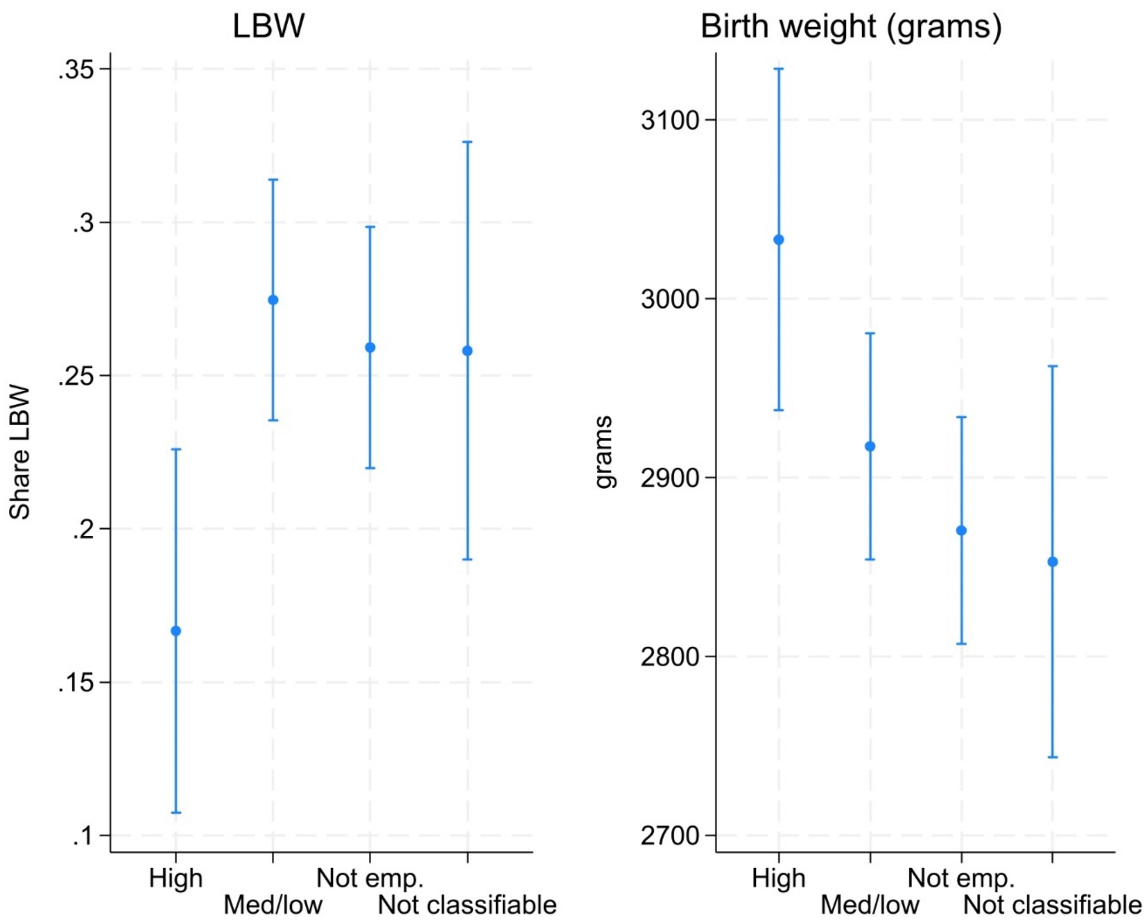
Table A4. Sensitivity analysis using SES in three categories

	(1)		(2)		(3)		(4)		(5)		(6)	
	Conception		Conception		Abortion		Abortion		Birth		Birth	
	AME	(SE)	AME	(SE)	AME	(SE)	AME	(SE)	AME	(SE)	AME	(SE)
Maternal SES												
High SES	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Med SES	0.020	(0.022)	0.019	(0.022)	-0.020	(0.035)	-0.016	(0.033)	0.021	(0.020)	0.019	(0.021)
Low SES	0.021	(0.060)	0.047	(0.062)	-0.113	(0.068)	-0.097	(0.070)	0.051	(0.057)	0.067	(0.060)
Not-employed	-0.002	(0.021)	-0.008	(0.023)	-0.003	(0.035)	0.019	(0.035)	-0.007	(0.019)	-0.015	(0.021)
Not class.	0.017	(0.029)	0.013	(0.028)	-0.070	(0.043)	-0.060	(0.042)	0.034	(0.027)	0.030	(0.027)
Marital Status												
Cohabiting			Ref.				Ref.				Ref.	
Single			-0.011	(0.179)			-0.041	(0.154)			0.057	(0.183)
Married			-0.009	(0.015)			-0.001	(0.024)			-0.009	(0.015)
Firstborn			-0.039*	(0.016)			-0.051*	(0.025)			-0.004	(0.016)
Age			-0.011***	(0.002)			0.006*	(0.003)			-0.010***	(0.002)
Nr. embryos.			0.120***	(0.014)			-0.019	(0.023)			0.106***	(0.013)
Technique Used												
IVF			Ref.				Ref.				Ref.	
IVF, ICSI			-0.045	(0.042)			0.084	(0.080)			-0.053	(0.039)
ICSI			-0.067*	(0.027)			0.031	(0.044)			-0.050*	(0.025)
IUI - hom.			0.175*	(0.072)			0.051	(0.112)			0.169*	(0.072)
IUI het.			-0.059	(0.055)			-0.135	(0.079)			0.004	(0.054)
FET			0.056*	(0.027)			-0.026	(0.043)			0.055*	(0.025)
First Treat.			0.000	(.)			0.000	(.)			0.000	(.)
Second			0.047**	(0.015)			-0.046*	(0.023)			0.048***	(0.014)
Third +			0.029	(0.021)			-0.025	(0.031)			0.028	(0.020)
Region of birth												
Abruzzo			Ref.				Ref.				Ref.	
Basilicata			-0.054	(0.086)			-0.140	(0.121)			-0.006	(0.088)
Calabria			-0.072	(0.078)			0.070	(0.113)			-0.076	(0.073)
Campania			-0.065	(0.070)			-0.085	(0.100)			-0.027	(0.069)
Emilia-Romagna			-0.083	(0.079)			-0.058	(0.114)			-0.054	(0.079)
Friuli-Venezia Giulia			-0.222	(0.250)			0.000	(.)			0.000	(.)
Lazio			-0.137	(0.071)			-0.089	(0.102)			-0.076	(0.069)
Liguria			-0.149	(0.092)			-0.183	(0.123)			-0.057	(0.091)
Lombardia			-0.062	(0.076)			-0.005	(0.111)			-0.020	(0.075)
Marche			-0.229*	(0.091)			-0.064	(0.152)			-0.157	(0.086)
Molise			-0.174	(0.113)			0.079	(0.197)			-0.161	(0.083)
Piemonte			-0.132	(0.080)			-0.010	(0.122)			-0.101	(0.075)
Puglia			-0.044	(0.080)			-0.119	(0.105)			0.003	(0.078)
Sardegna			-0.213*	(0.089)			-0.108	(0.137)			-0.151	(0.084)
Sicilia			-0.022	(0.075)			-0.080	(0.107)			0.005	(0.075)
Toscana			-0.084	(0.066)			-0.045	(0.094)			-0.047	(0.065)
Trentino Alto Adige			-0.131	(0.337)			0.000	(.)			0.017	(0.337)
Umbria			-0.187*	(0.092)			-0.097	(0.137)			-0.126	(0.088)
Veneto			-0.066	(0.090)			-0.122	(0.122)			0.015	(0.085)
Foreign born			-0.125	(0.067)			-0.077	(0.096)			-0.068	(0.066)
Year of birth												
2016 (Ref.)			Ref.				Ref.				Ref.	
2017			0.040	(0.026)			0.078	(0.040)			-0.000	(0.026)
2018			0.055*	(0.028)			0.058	(0.042)			0.027	(0.026)
2019			0.012	(0.028)			0.046	(0.042)			0.005	(0.027)
2020			-0.008	(0.029)			0.073	(0.047)			-0.017	(0.028)
2021			0.045	(0.029)			0.020	(0.043)			0.046	(0.029)
N	4,747		4,747		1,597		1,595[b]		4,747		4,743[a]	

Note: AME are obtained from logistic models. Columns (1, 3, 5) report baseline models; columns (2, 4, 6) report adjusted models. [a] We lose four cases for collinearity between Friuli Venezia Giulia and control variables. [b] We lose two cases for collinearity between region of birth (Friuli Venezia Giulia, Trentino AA) and other control variables.

Figures

Figure A1. Validation of SES measurement on newborn's birth weight (on the right) and newborn's low birth weight (LBW; on the left)



Note: predicted values and probabilities are obtained by estimating a linear regression (right-panel) and a logistic regression (left-panel) on birth weight using SES as a predictor.