The impact of consumer affordability on access to assisted reproductive technologies and embryo transfer practices: an international analysis

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Objective: To systematically quantify the impact of consumer cost on assisted reproduction technology (ART) utilization and numbers of embryos transferred.
Design: Ordinary least squared (OLS) regression models were constructed to measure the independent impact of ART affordability—measured as consumer cost relative to average disposable income—on ART utilization and embryo transfer practices.
Setting: Not applicable.
Patient(s): Women undergoing ART treatment.
Intervention(s): None.
Main Outcome Measure(s): OLS regression coefficient for ART affordability, which estimates the independent effect of consumer cost relative to income on utilization and number of embryos transferred.
Result(s): ART affordability was independently and positively associated with ART utilization with a mean OLS coefficient of 0.032. This indicates that, on average, a decrease in the cost of a cycle of 1 percentage point of disposable income predicts a 3.2% increase in utilization. ART affordability was independently and negatively associated with the number of embryos transferred, indicating that a decrease in the cost of a cycle of 10 percentage points of disposable income predicts a 5.1% increase in single-embryo transfer cycles.
Conclusion(s): The relative cost that consumers pay for ART treatment predicts the level of access and number of embryos transferred. Policies that affect ART funding should be informed by these findings to ensure equitable access to treatment and clinically responsible embryo transfer practices. (Fertil Steril® 2014;101:191–8. ©2014 by American Society for Reproductive Medicine.)
Key Words: Assisted reproductive technology, cost analysis, insurance mandates, single-embryo transfer

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Assisted reproductive technology (ART) has evolved over the last 3 decades into mainstream treatments for infertility. It is estimated that 5 million children have been born following ART worldwide, including up to 5% of all children is some countries (1, 2). However, striking international differences exist in the utilization of ART and embryo transfer practices, even among developed countries where the prevalence of infertility is similar (3). Such disparities reflect differences in funding, regulatory environments, and sociocultural norms (4). One of the most notable disparities exists between the Nordic countries and the United States (U.S.). The Nordic countries are considered to be world leaders in ART, with 2.5 times more ART cycles performed per woman of reproductive age than in the U.S., and single-embryo transfer (SET) performed in 56% of fresh embryo treatment cycles compared with 13% in the U.S. (2, 5). One obvious difference between these fertility markets is that most European health care systems provide some level of public funding for ART, whereas the U.S. has no public funding and comprehensive insurance mandates to cover ART treatments in only five states. This situation prevents many couples in the U.S. from receiving treatment and creates a financial incentive to transfer multiple embryos to maximize the chance of pregnancy. Such differences not only have profound implications on equity of access to fertility treatment, but also create a high iatrogenic risk for ART children being born as twins or triplets and therefore undeniably poorer outcomes for ART children (6, 7).

The present study is the first analysis comparing international data from a range of countries and jurisdictions with diverse financing and regulatory environments to evaluate and quantify the impact of consumer cost, health care system characteristics, and sociodemographic factors on access to ART and embryo transfer practices. Our findings can help inform polices regarding funding for ART.

DESIGN AND METHODS

Data Sources

ART treatment, health care system, and sociodemographic data were collected from 30 high and upper middle income countries with a gross domestic product (GDP) of at least USD 8,800 per capita. The U.S. was included using a representative sample of states with and without insurance mandates to cover ART: U.S. states with comprehensive insurance mandates were represented by Connecticut, Massachusetts, and New Jersey; and U.S. states without insurance mandates were represented by Michigan, Oregon, and Washington. Treatment data were mainly sourced from national ART registries either directly from public reports or via requests to ART registry data custodians. Health care and sociodemographic data were obtained from international and national agencies, including the Organisation for Economic Cooperation and Development (OECD), The World Bank, and national statistics offices and bureaus. The cost of ART treatment and charges to patients were derived from previously published estimates and clinic surveys. All data were from 2006–2007 unless otherwise stated, because there is a lag of up to 5 years between ART treatment and the release of ART registry data. Data for countries reporting less than 100% of cycles were proportionally estimated, and missing data were imputed with the use of regression estimates. Health care costs were converted from local currencies to constant USD2006 with the use of OECD purchasing power parities and the health care price deflators supplied by each country's national statistics office. The list of countries and states, data values, and data sources used in the analysis are supplied in detail in Supplemental Table 1 (available online at www.fertstert.org).

Empirical Models

These data were used to construct four ordinary least squared (OLS) econometric regression models to systematically measure the impact of consumer cost relative to income, health care system characteristics, and sociodemographic factors on access to ART treatment and embryo transfer practices. All analyses were performed with the use of Stata 11 (Stata Corp.). Access to ART treatment was represented by a Utilization outcome (dependent) variable, measured as the number of fresh nondonor cycles per million women of reproductive age. Variation in clinical practice was represented by three embryo transfer outcome variables: the average number of embryos transferred in fresh ART cycles (average embryos), the percentage of fresh single-embryo transfer cycles (% SET), and the percentage of fresh cycles transferring three or more embryos (% $\geq$3 embryos). The explanatory (independent) variable of interest in all models was affordability, representing the net cost to patients of a fresh in vitro fertilization (IVF) cycle after government or third-party subsidies as a percentage of disposable income of a single person without dependents earning 100% of the average wage in their country. Disposable income was calculated with the use of OECD methods (8). The affordability variable is therefore a composite variable incorporating the cost of treatment, level of subsidization of ART treatment, and disposable income levels within each country and reflects the economic burden faced by patients to pay for ART treatment. After controlling for other explanatory variables, affordability was hypothesized to be the most important economic driver influencing patients' access to ART treatment and clinical practice.

To explain additional variation in access to treatment among countries, the Utilization model included the following ten explanatory variables: the potential level of clinic access to women of reproductive age, physicians per population, measures of pronatality (total fertility rate and mean age at first childbirth), measures of economic development (urbanization, gross national income [GNI] per capita, infant mortality rate), characteristics of health care financing (proportion of GDP spent on health, proportion of total health expenditure paid as patient out-of-pocket costs [OOP]), and ART clinical pregnancy rates. To explain additional variation in clinical practice, the three embryo transfer models included three further explanatory variables: a proxy for implantation rate, the age distribution of women undergoing ART treatment, and a binary variable to indicate whether public funding was linked to SET (funding linked to SET). Each explanatory variable was chosen because of its potential to have an independent and exogenous effect on the outcome variables (i.e., utilization, average embryos, %SET, % $\geq$ 3 embryos). Therefore, controlling for the explanatory variables in the models allows the effect of affordability on the outcome variables to be isolated. For example, high clinical pregnancy rates (especially if published) could increase utilization independently from the effect of consumer cost. The four outcome variables and explanatory variables are described in Table 1, and the value of each of these variables for each country and state is detailed in Supplemental Table 1 (available online at www.fertstert.org).

The data used to construct the OLS models provide estimates (represented as coefficients) of the relationship between each of the explanatory variables and the four outcomes of interest (one utilization and three clinical practice variables). The sign and magnitude of an explanatory variable's coefficient determines how the value of the outcome variable is predicted to change as the value of an explanatory variable varies while controlling for all other explanatory variables. Therefore, the coefficient for affordability captures the independent association between consumer cost and ART utilization and clinical practice after controlling for other explanatory variables. The relationship between the outcome variable and explanatory variables, specifically whether it is linear or logarithmic, and the units of measurements determines how each coefficient is interpreted. The Utilization model is expressed as a log-linear model, meaning that a 1-unit change in the coefficient of an explanatory variable predicts the equivalent percentage change in the outcome variable. The clinical practice models are expressed as linear-linear models, meaning that a 1-unit change in the coefficient of an explanatory variable predicts a 1-unit change in the outcome variable.

The value of the OLS coefficient reflects the mean relationship between the outcome variable and the set of explanatory variables and is reported as the OLS coefficients. Because the effect of the explanatory variables can vary in both magnitude and significance across different values (percentiles) of the outcome variables, quantile OLS coefficients are also reported across the range of utilization rates and embryo transfer practices. This enables a much richer understanding of the relationship between explanatory variables and the outcomes of interest.

Our approach to the analysis was to use stepwise regressions starting with affordability and sequentially adding the explanatory variables, omitting explanatory variables that were not statistically significant. This approach allowed us to test the robustness of the estimated coefficients for affordability by observing if the affordability coefficient altered substantially under various model specifications owing to the inclusion of irrelevant variables or measurement error, as well as to build a model that included only relevant variables, thus minimizing the standard error (SE). In addition,

TABLE 1

Definitions of dependent and explanatory variables and summary statistics (2006-07).

Variable	Measure	n	Mean	SD	Min.	Max.
Utilization[a]	No. of fresh nondonor cycles per million women of reproductive age (aged 15–49 y)	31	3,245	1,923	466	7,979
Clinical practice[a]	Average no. of embryos transferred in fresh nondonor cycles (average embryo)	28	2.09	0.53	1.30	3.54
	Percentage of fresh nondonor cycles that were SET (%SET)	28	24.78	20.07	1.50	69.9
	Percentage of fresh nondonor cycles transferring $\geq$3 embryos (% $\geq$ 3 embryos)	26	25.08	24.54	0	77.6
Affordability[b]	Net cost of a standard IVF cycle divided by annual disposable income for a single person earning 100% of average wages with no dependents (%)	31	16.72	13.04	2.26	52.36
Clinic access[b]	ART clinics per million women of reproductive age	31	8.56	5.47	1.059	21.79
Physicians[b]	Practicing physicians per 10,000 people	31	29.87	8.89	12	50
Pronatality[b]	Total fertility rate: no. of children born to women aged 15–49 y	31	1.69	0.31	1.12	2.3
	Mean age of women at first childbirth	31	27.55	1.67	21.3	29.8
Economic development[b]	Level of urbanization: percentage of a country's population living in metropolitan areas	31	35.23	25.04	4	92.9
	Gross national income (GNI) per capita	31	30,794	10,900	8,810	53,368
	Infant mortality rate: deaths per 1,000 live births	31	5.86	5.04	1.4	22.3
Health care financing[b]	Total expenditure on health as a percentage of gross domestic product (GDP)	31	9.01	1.89	5.7	13.7
	Out-of-pocket health expenses as a percentage of total expenditure on health	31	21.49	12.88	5.6	63.8
Implantation rate[b]	Proxy for implantation rate: no. of babies delivered divided by no. of embryos transferred in fresh cycles (%)	27	15.31	4.45	8	25.3
Clinical pregnancy rate[b]	No. of clinical pregnancies per initiated fresh cycle (%)	31	28.79	4.51	18.85	38.89
Age distribution[b]	Percentage of fresh cycles undertaken by women aged >35 y	26	0.51	0.1	0.328	0.733
Funding linked to SET[b]	Binary variable set to 1 if funding linked to SET	32	0.09	0.29	0	1

Note: ART = assisted reproductive technologies; SET = single-embryo transfer.
[a] Outcome (dependent) variables.
[b] Explanatory (independent) variables.

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we performed a range of other robustness checks of the four models, including preestimation correlation matrices to detect multicollinearity between explanatory variables, and the use of robust SEs to deal with possible violations of the error term (Huber-White sandwich estimators). The robustness of the four models was also tested by omitting data from countries reporting <50% of cycles. Similarly the robustness of the % SET model was tested by omitting U.S. state data because due to source data representation, "elective" SET, rather than all SET, was used for U.S. states. The overall explanatory power of the each of the four final models is described by R^2, which quantifies the proportion of the variation in the outcome variable that is explained by the explanatory variables, and the F-statistic, which tests the overall statistical significance of the model. Because each country and state represent different size populations we also reported all regression analyses with the use of weighted observations based on number of ART cycles performed. However, because policy decisions about ART funding are made at the national or state levels, we favor the use of the unweighted models for informing policy.

RESULTS

Access to ART Treatment (Utilization)

The number of fresh cycles per million women of reproductive age ranged from 466 in Brazil to 7,979 in Denmark, with a mean among all countries of 3,245 (Table 1). The relationship between utilization and affordability for each country and the overall linear trend is plotted in Figure 1A.

The OLS regression model showed that there was a statistically significant and robust association between the variation in utilization and affordability after controlling for other explanatory variables (Table 2). The explanatory variables clinic access and physicians were also independently associated with Utilization. Approximately 80% of the variation in utilization was jointly explained by the explanatory variables ($R^2 = 0.79$), and the overall model was highly significant ($P < .01$).

After controlling for explanatory factors, the mean coefficient of affordability was −0.032 ($P < .01$), indicating that, on average, a 1-percentage-point decrease in consumer affordability predicts an average decrease in ART utilization of 3.2%. For example, at the mean value of affordability, the net cost of a fresh IVF cycle to a patient accounts for 16.7% of average annual disposable income (Table 1). A 10-percentage-point decrease in affordability at this level would mean that the net cost of an ART cycle accounts for 26.7% of annual disposable income. Because the Utilization model is log-linear, this would predict a 32% decrease in ART utilization from the mean of 3,245 fresh cycles per million women of reproductive age to 2,197 fresh cycles per million women of reproductive age.

As an additional verification of the above finding, disposable income, OOP per fresh cycle, and an interaction term for disposable income and OOP per fresh cycles were introduced into the model (rather than as a proportion represented by affordability) to test for the effect of OOP on utilization at different levels of income (coefficients: OOP 0.0235; disposable income −0.2058; OOP × disposable income 0.0035). The coefficients for the OOP and interaction term were jointly different from zero (joint F-statistic = 12.69; $P < .001$). This confirms our intuition that the impact of OOP for ART treatment varies by the level of disposable income within a country or state and thus justifies the use of the composite measure of affordability to reflect consumer cost of IVF treatment relative to disposable income. Reparameterizing the model indicates that a USD1,000 increase in OOPs for a fresh IVF cycle predicts a 12.45% decrease in utilization ($P < .001$) at the average value for disposable income (USD22.61K). This finding is consistent with the conclusion that the economic burden faced by consumers is associated with lower utilization.

Similarly, the coefficient of clinic access was 0.042 ($P < .01$), suggesting that, on average, for every additional ART clinic per million women of reproductive age, ART utilization is predicted to increase by 4.2%. The coefficient of the number of physicians per capita also was significant at 0.021 ($P < .01$), indicating that, on average, as the concentration of physicians increases within a country, so does the predicted utilization of ART treatments (Table 2).

The quantile regression showed that the coefficient of affordability was negative over all ranges of utilization, with a larger effect at the lower and higher quantiles, indicating that ART utilization is more sensitive to changes in cost at higher and lower levels of existing ART utilization (Supplemental Fig. 1A is available online at www.fertstert.org).

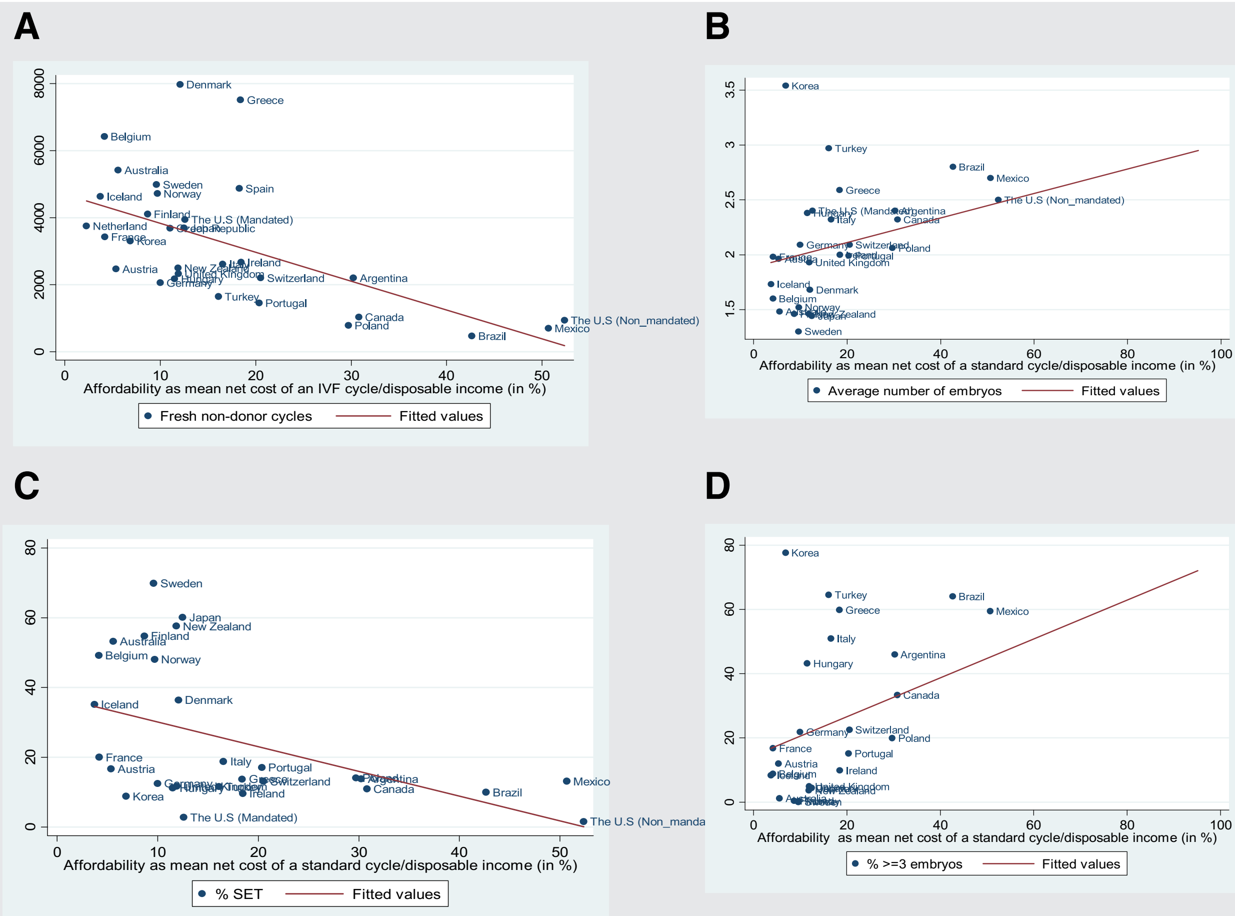
Embryo Transfer Practices

The percentage of fresh cycles in which a single embryo was transferred ranged from <2% in U.S. states (elective SET) without mandates to 70% in Sweden (mean 24.8%), and the percentage of fresh cycles in which three or more embryos were transferred ranged from 0% in Sweden to 78% in South Korea (mean 25.1%). The average number of embryos transferred ranged from 1.30 to 3.54 (mean 2.09; Table 1). The relationship between the three clinical practice outcome variables and affordability for each jurisdiction and the overall linear trends are plotted in Figures 1B–1D.

The OLS regression models showed that there was a statistically significant association between the variation in embryo transfer practices and affordability after controlling for other explanatory variables. Approximately 50%–60% of the variation in clinical practice was jointly explained by the explanatory variables ($R^2 = 0.50$–0.61), and the overall models were highly significant ($P < .01$; Table 3). There existed a highly significant association between affordability and the clinical practice outcome variables during the stepwise regression process, indicating a robust association. The model and coefficients remained significant after restricting the model to countries with >50% of cycles reported and after removing U.S. state data from the models.

After controlling for explanatory variables, the mean coefficient for affordability was 0.014 ($P < .01$) for the Average Embryo model, indicating that a 10-percentage-point decrease in affordability (e.g., an increase in the cost of an IVF cycle from 16.7% to 26.7% of annual disposable income) would predict an

FIGURE 1



Scatterplots of outcome variables and affordability (2006 - 2007). (A) Correlation between affordability and utilization (number of fresh nondonor cycles per million women of reproductive age [15–49 y]). Correlation coefficient = −0.35. (B) Correlation between affordability and average number of embryos transferred in fresh nondonor cycles. Correlation coefficient = 0.45. (C) Correlation between affordability and percentage of fresh nondonor embryo transfer cycles in which a single-embryo was transferred (SET). U.S. state data represent "elective" SET; all other jurisdictions represent SET. Correlation coefficient = −0.44. (D) Correlation between affordability and percentage of fresh nondonor embryo transfer cycles in which three or more embryos were transferred. Correlation coefficient = 0.52.

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average increase of 0.14 embryos transferred in each fresh cycle. Similarly, a 10-percentage-point decrease in affordability would predict a 5.1-percentage-point decrease in the percentage of fresh SET cycles ($P<.01$) and a 7.5-percentage-point increase in the percentage of fresh cycles transferring ≥ 3 embryos ($P<.01$). The explanatory variable, implantation rate, was also independently and negatively associated with the average number of embryos transferred ($P<.05$) and the percentage of fresh cycles having ≥ 3 embryos transferred ($P<.01$). This indicates that, after controlling for all other explanatory variables, if the implantation rate, as measured in this study, increases by 10 percentage points, it is predicted that the average number of embryos transferred in a fresh cycle would decrease by 0.52 embryos. As would be expected, policies linking funding to SET (funding linked to SET) were independently and positively associated with the percentage of cycles transferring a single embryo ($P<.05$; Table 3).

The quantile regression for the three clinical practice models found that the association between affordability and embryo transfer practices was strongest in countries with relatively low numbers of embryos already being transferred per cycle. That is, there was a significant and positive association between affordability and a lower number of embryos transferred up to the 75th percentile of countries as measured by the number of embryos transferred per cycle (Average Embryos and ≥ 3 Embryos models). Similarly, there was a significant association only between affordability and %SET above the 90th percentile measured by the %SET cycles (Supplemental Figs. 1B–1D). This indicates that, after controlling for implantation rate and policies which explicitly link funding to SET, embryo transfer practices are more sensitive to changes in cost in jurisdictions that already transfer low numbers of embryos per cycle. Conversely, the models indicate that jurisdictions that currently transfer high numbers

TABLE 2

Ordinary least squares regression analysis of utilization: log-linear equations.

Variable	Coefficient (robust SE)	*P* value	Weighted coefficient[a] (robust SE)	*P* value[a]
Affordability	−0.032 (0.005)	<.01	−0.026 (0.003)	<.001
Physicians per 10,000 population	0.021 (0.007)	<.01	0.020 (0.010)	NS
ART clinics per million women of reproductive age	0.042 (0.011)	<.01	0.016 (0.02)	NS
Total fertility rate	0.392 (0.200)	<.1	0.422 (0.182)	<.05
Clinical pregnancy rate	–	NS	NS	NS
Mean age at first childbirth	–	NS	NS	NS
Level of urbanization	–	NS	NS	NS
GNI per capita	–	NS	NS	NS
Total mortality rate	–	NS	NS	NS
Health expenditure/GDP	–	NS	NS	NS
Out-of-pocket payments/health expenditure	–	NS	NS	NS
Constant	6.757 (0.439)		6.735 (0.426)	
No. of observations	31		31	
R^2	0.79		0.84	
F-statistic	26.54	<.01	45.8	<.01

Note: Dependent variable is fresh nondonor cycles per million women of reproductive age (Utilization). The utilization model includes 31 jurisdictions: Argentina, Australia, Austria, Belgium, Brazil, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, South Korea, Mexico, The Netherlands, New Zealand, Norway, Poland, Portugal, Spain, Sweden, Switzerland, U.S. (states with comprehensive ART insurance mandated: Connecticut, Massachusetts, New Jersey), U.S. (states without ART insurance mandates: Michigan, Oregon, Washington), Turkey, and United Kingdom. NS = not statistically significant; SE = standard errors.
[a] Observations weighted according to number of fresh ART cycles undertaken in a country of state.

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of embryos would be relatively resistant to transferring fewer embryos even when incentivized by lower costs to consumers.

DISCUSSION

This is the first international study of ART treatment to quantify the impact of consumer cost on access to ART treatment and embryo transfer practices. The analysis found that the average cost that patients pay for treatment relative to their income (measured by the affordability variable) is significantly associated with not only who has access to treatment but also the way in which ART is practiced.

After controlling for other explanatory variables, affordability had a strong and robust association with utilization, with a 10-percentage-point decrease in affordability predicted to, on average, decrease utilization by 32%. This is in line with what has been experienced by countries such as Germany, Denmark, and Australia when public ART funding was restricted (9–11).

Because of the high cost of health care in the U.S. and the lack of financial support for ART treatment in states without ART insurance mandates, the majority of the U.S. has the most expensive ART in the world. One fresh IVF cycle accounts for 52% of an individual's average disposable income in states without ART insurance mandates, compared with 13% for states with mandates and <10% in many of the other high and upper middle income countries included in this study.

Uptake of ART treatment was more sensitive to changes in cost at both lower levels of existing utilization, where there is likely pent up demand for ART treatment, and upper levels of existing utilization, where there is potentially excess use of ART treatment. These findings are consistent with studies that suggest the demographic profile of women accessing ART treatment changes with the level of financial access. Studies using U.S. data found that patients who seek treatment in response to lower ART cost in mandated states may include those with both better and poorer prognoses from ART treatment (12–14). In theory this occurs because as the price a patient pays decreases, the cost of treatment becomes equivalent to the expected benefit they will obtain from ART treatment. That is, if ART treatment becomes more affordable, women with a relatively high probability of natural conception without ART are more likely to seek treatment (e.g., younger patients), as are women with a low probability of ART success (e.g., older patients). A recent policy analysis of a reduction in ART public funding in Australia supports this finding by demonstrating that relatively more older women discontinued treatment as affordability decreased, presumably because of their poorer prognosis and therefore lower expected benefit from treatment (9). The number of clinics per woman of reproductive age was also independently associated with ART utilization, pointing to degree of supplier-induced demand in the ART market.

Affordability was also independently and significantly associated with the number of embryos transferred, with higher numbers of embryos transferred in jurisdictions with relatively expensive ART. This is also consistent with findings from the U.S. showing that states with insurance mandates transfer lower numbers of embryos (13, 15–17). However, although the overall association between affordability and embryo transfer practices was significant, our study findings indicate that embryo transfer practices are more sensitive to changes in cost in jurisdictions which already transfer low numbers of embryos per cycle. That is, a relatively larger fall in consumer cost would be needed to drive more conservative embryo transfer practices in jurisdictions with already high numbers of embryos being transferred, such as U.S. states without mandates. One explanation for this is that where it is mandatory to report highly publicized clinic-specific pregnancy rates, such as in the U.S., the market incentive to attract patients overrides the incentive for conservative

TABLE 3

Ordinary least squares regression analysis of ART embryo transfer practices. Linear-linear equations.

Variable	Average embryo model Coefficient (robust SE)	Average embryo model P value	Average embryo model (weighted)[a] Coefficient (robust SE)	Average embryo model (weighted)[a] P value	%SET model Coefficient (robust SE)	%SET model P value	%SET model (weighted)[a] Coefficient (robust SE)	%SET model (weighted)[a] P value	%≥3 embryo model Coefficient (robust SE)	%≥3 embryo model P value	%≥3 embryo model (weighted)[a] Coefficient (robust SE)	%≥3 embryo model (weighted)[a] P value
Affordability	0.014 (0.005)	<.01	0.014 (0.001)	<.01	−0.51 (0.173)	<.01	−0.632 (0.076)	<.001	0.748 (0.252)	<.01	0.525 (0.211)	<.05
Implantation rate	−0.052 (0.022)	<.05	−0.038 (0.01)	<.01	0.905 (0.751)	NS	1.568 (0.323)	<.001	−3.192 (0.925)	<.01	−1.927 (0.764)	<.05
Funding linked to SET	−0.24 (0.127)	<.1	−0.209 (0.085)	<.05	27.367 (7.714)	<.05	21.73 (0.127)	<.001	4.463 (7.185)	NS	0.778 (5.103)	NS
Patients >35 y (%)	–	NS	–	NS	–	NS	–	NS	–	NS	–	NS
Constant	2.646 (0.456)		2.409 (0.213)		17.27 (12.491)		6.95 (6.322)		58.936 (19.862)		42.45 (15.67)	
No. of observations	27		27		27		27		25		27	
R^2	0.5		0.72		0.51		0.7376		0.61		0.57	
F-statistic	42.92	<.01	77.32	<.01	26.16	<.01	54.82	<.01	43.38	<.01	11.99	<.01

Note: The average embryo and %SET models include 27 jurisdictions: Argentina, Australia, Austria, Belgium, Brazil, Canada, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, South Korea, Mexico, New Zealand, Norway, Poland, Portugal, Sweden, Switzerland, U.S. (states with comprehensive ART insurance mandated: Connecticut, Massachusetts, New Jersey), U.S (states without ART insurance mandates: Michigan, Oregon, Washington), and United Kingdom. The %≥3 embryo model includes the same jurisdictions as above except the U.S. NS = not statistically significant; SE = standard errors; SET = single-embryo transfer.

[a] Observations weighted according to number of fresh ART cycles undertaken in a country of state.

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embryo transfer practices. With so few states having mandates for insurance coverage, the overriding competitive nature of the private ART market across the U.S. likely limits the impact of the lower patient costs in mandated states.

The importance of increasing the use of SET in properly selected patients is now well established on clinical and cost-effectiveness grounds (18–20). Several national reproductive medicine societies have clinical practice guidelines and education campaigns emphasizing the important role of SET (21–26). Moreover, a number of jurisdictions, such as Belgium, Turkey, and Quebec, fund ART only if such guidelines are followed, which has led to a significant reduction in multiple birth rates in those jurisdictions (27–29). However, Australia, Finland, and Japan also have been able to achieve multiple birth rates of <10% through supportive public funding and patient and clinician education, thereby conserving clinician and patient autonomy (30–32).

A limitation of the present study is that the nexus between socioreligious/cultural factors and ART utilization was not well captured owing to the difficulty in quantifying such factors. For example, the Catholic Church opposes artificial procreation, but it was not possible to isolate the religious impact in countries influenced by Catholic traditions and teachings from other explanatory variables. Furthermore, this model was necessarily based on cross-sectional data from 2006–2007 and therefore should be interpreted with caution in terms of inferring causality. Even though there was a stable and statistically significant effect between affordability and ART utilization and clinical practice under all model specifications, cross-sectional data cannot prove causal relationships between explanatory and outcomes variables. Also worth noting is that because we use aggregate data at a particular point in time, the behavior of all individuals within a country or state would not be reflected by the models, nor would changes in attitudes over time of clinicians or patients, e.g., attitudes towards SET and seeking treatment for fertility problems.

In conclusion, as utilization and applications of ART expand worldwide—owing to both the increasing effectiveness of treatment and increasing rates of subfertility as couples delay childbirth—public policies must be informed by the impact that financing arrangements have on the behavior of consumers and clinicians. The application of this knowledge alongside clinical and patient education programs is important to ensure not only equitable access to treatment but clinically responsible embryo transfer practices that result in the best possible outcomes for infertile patients and ART children.

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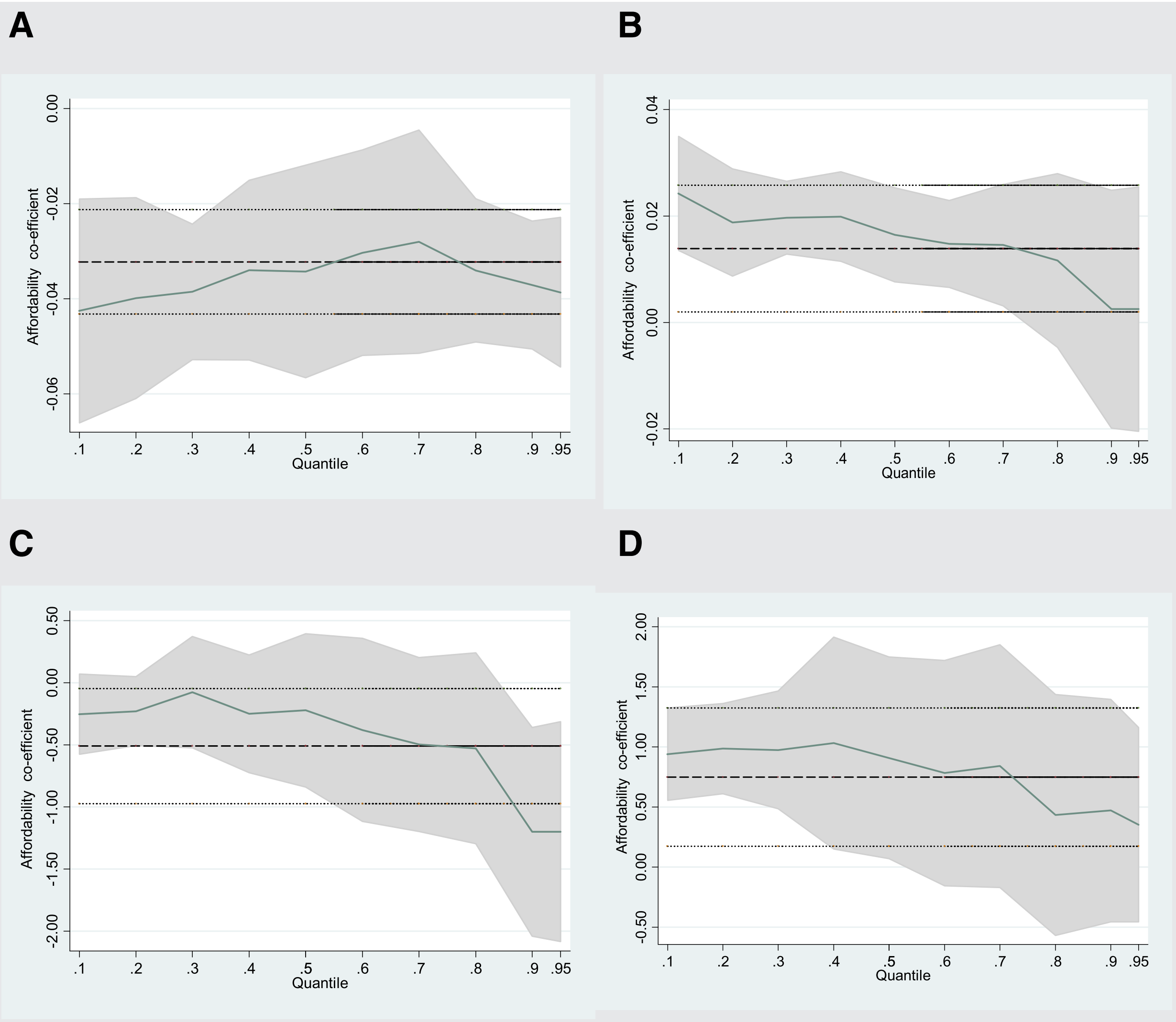
SUPPLEMENTAL FIGURE 1



Quantile regressions and confidence intervals for the outcome variables and affordability (2006 to 2007). (A) Quantile regression for utilization (number of fresh nondonor cycles per million women of reproductive age [15–49 y]) and affordability. The coefficients were significant ($P<.01$) at all values of Utilization, with the affordability coefficients ranging from −0.042 at the 10th percentile to −0.032 at the 75th percentile. (B) Quantile regression for average number of embryos transferred in fresh cycles and affordability. The affordability coefficients were significant ($P<.01$) at the 10th percentile (coefficient = 0.024) through to the 75th percentile (coefficient = 0.014). (C) Quantile regression for percentage of fresh cycles transferring a single embryo and affordability. The coefficients were significant ($P<.01$) at the lower and upper percentiles but not for the 25th through to the 75th percentiles. 10th percentile coefficient = −0.025; 90th percentile coefficient = −1.200. (D) Quantile regression for percentage of fresh cycles with three or more embryos and affordability. The coefficients were significant at the 10th percentile (coefficient = 0.938; $P<.01$) through to the 75th percentile (coefficient = 0.792; $P<.05$), but not at the 90th percentile.

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Countries, data values, and data sources.

		Outcome (dependent) variables				Explanatory (independent) variables					
Country	**Source of ART treatment data**	**Fresh nondonor cycles per million women of reproductive age (15–49 y)**	**Average no. of fresh nondonor embryos per fresh embryo transfer cycle**	**% SET nondonor fresh embryo transfer cycles**	**% ≥3 fresh nondonor embryo transfer cycles**	**Affordability (net cost of a fresh ART cycle as % of annual disposable income)**	**Average disposable income for a single worker without dependents earning 100% average wage USD2006[a]**	**Average gross cost of an ART cycle USD2006[b]**	**Average net cost to consumers (out-of-pocket costs) of a fresh ART cycle USD2006[b]**	**No. of ART clinics per million women of reproductive age (15–49 y)[c]**	**No of physicians per 10,000 population[c]**
Australia	ICMART[f]	5,416	1.48	53.2	1.1	5.58	29,314	5,641	1,636	4.94	25
Austria	ESHRE[g]	2,469	1.96	16.6	11.9	5.37	26,508	4,748	1,424	12.47	37
Belgium[m]	ESHRE[g]	6,418	1.60	49.2	8.8	4.14	24,484	3,245	1,013	7.43	42
Canada	CFAS[h]	1,030	2.32	10.9	33.3	30.81	24,537	8,495	7,561	3.11	19
Czech Republic	ESHRE[g]	3,681	N/A	N/A	N/A	11.00	12,500	2,750	1,375	8.38	36
Denmark	ESHRE[g]	7,979	1.68	36.4	4.2	12.06	22,867	5,513	2,757	17.67	36
Finland	ESHRE[g]	4,101	1.46	54.7	0.3	8.67	24,983	5,452	2,166	15.46	33
France	ESHRE[g]	3,426	1.98	20	16.7	4.18	24,807	3,453	1,036	6.88	34
Germany	ESHRE[g]	2,051	2.09	12.4	21.8	9.98	25,711	5,130	2,565	6.29	34
Greece	ESHRE[g]	7,519	2.59	13.7	59.8	18.40	23,075	4,818	4,245	19.28	50
Hungary	ESHRE[g]	2,172	2.38	11.2	43.2	11.51	9,646	3,700	1,110	4.16	30
Iceland	ESHRE[g]	4,628	1.73	35.1	8.3	3.70	26,257	4,856	971	13.37	38
Ireland	ESHRE[g]	2,669	2.00	9.5	9.8	18.47	25,335	5,400	4,680	6.18	29
Italy	ESHRE[g]	2,607	2.32	18.7	50.9	16.54	20,049	4,146	3,317	14.28	37
Japan[n]	JSOG[i]	3,696	1.44	60.1	4.38	12.49	31,662	3,955	3,955	21.79	21
Korea	KSOG[j]	3,303	3.54	8.8	77.6	6.86	32,810	3,000	2,250	10.88	16
Mexico	REDLARA[k]	691	2.70	13.07	59.42	50.68	9,372	5,000	4,750	5.73	20
Netherlands	ESHRE[g]	3,751	N/A	N/A	N/A	2.26	27,236	3,077	615	3.28	37
New Zealand	ICMART[f]	2,499	1.46	57.6	3.6	11.85	23,213	5,500	2,750	3.93	21
Norway	ESHRE[g]	4,714	1.52	48	0.2	9.70	28,426	5,513	2,757	10.25	38
Poland	ESHRE[g]	782	2.06	14	19.9	29.71	10,770	3,200	3,200	3.22	20
Portugal	ESHRE[g]	1,453	1.99	17	15.1	21.26	16,466	5,000	3,354	8.15	34
Spain	ESHRE[g]	4,867	N/A	N/A	N/A	18.28	21,442	5,600	3,920	16.01	33
Sweden	ESHRE[g]	4,986	1.30	69.9	0	9.61	24,172	4,648	2,324	6.92	33
Switzerland	ESHRE[g]	2,199	2.09	13.1	22.5	20.53	32,476	6,667	6,667	13.00	40
Turkey[o]	ESHRE[g]	1,646	2.97	11.5	64.5	16.09	14,296	4,600	2,300	3.86	16
United Kingdom	ESHRE[g]	2,322	1.93	11.6	4.8	11.89	36,468	5,780	4,335	4.81	23
United States	CDC/ASRM/SART[l]	1,532	2.48	10.7	43.2	46.08	24,917	13,048	11,482	6.58	26
U.S. states (mandates)[q]	CDC/ASRM/SART[l] plus clinic survey	3,944	2.40	2.7	na	12.57	24,917	13,048	3,131	6.50	26
U.S. states (nonmandated)[r]	CDC/ASRM/SART[l] plus clinic survey	932	2.50	1.5	na	52.36	24,917	13,048	13,048	4.09	26
Brazil	REDLARA[k]	466	2.80	9.91	64.06	42.67	8,719	4,000	3,720	1.06	12
Argentina	REDLARA[k]	2,203	2.40	13.73	45.97	30.25	13,553	4,100	4,100	2.04	30

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SUPPLEMENTAL TABLE 1

Continued.

Country	Total fertility rate[c]	Mean maternal age at first childbirth (2005 data)[d]	Level of urbanization[e]	GNI per capita (USD2006)[e]	Total infant mortality rate[c]	Health expenditure/ GDP[c]	Out-of-pocket expenditure/ total health expenditure[c]	Proxy for implantation rate (% babies/ embryos tranferred in fresh cycles)	ART clinical pregnancy rate (clinical pregancies/ initiated fresh ART cycle)	Percentage of ART patients aged $\geq$35 y	Policy linking ART funding to SET. 1 = policy exists[b]
Australia	1.82	28.0	60	34,113	1.82	8.5	18.70	19.17	23.81	0.60	0
Austria	1.41	27.2	20	34,920	1.41	10.3	15.80	11.21	31.67	N/A	0
Belgium[m]	1.8	27.4	18	33,656	1.8	9.5	18.80	14.34	27.47	0.43	1
Canada	1.59	27.6	43	36,451	1.59	10	14.90	17.64	33.66	0.56	0
Czech Republic	1.33	26.9	11	20,743	1.33	7	11.30	N/A	34.58	0.33	0
Denmark	1.85	28.4	21	35,839	1.85	9.6	14.30	17.22	26.12	0.45	0
Finland	1.84	27.9	20	32,907	1.84	8.4	19.00	17.75	26.24	0.44	0
France	1.98	28.5	23	31,120	1.98	11.1	7.00	14.73	25.20	0.43	0
Germany	1.33	28.1	8	33,602	1.33	10.5	13.40	11.09	27.26	0.52	0
Greece	1.41	28.5	29	25,787	1.41	9.7	36.02	8.96	25.28	0.62	0
Hungary	1.35	26.7	17	16,882	1.35	8.1	23.00	14.19	28.80	0.39	0
Iceland	2.07	26.3	92.9	32,309	2.07	9.1	16.60	19.83	30.35	0.54	0
Ireland	1.9	28.5	25	35,873	1.9	7.5	14.50	16.98	25.35	0.69	0
Italy	1.35	28.7	17	29,467	1.35	9	19.90	7.95	18.85	0.62	0
Japan[n]	1.32	29.1	48	32,843	1.32	8.1	15.10	10.08	22.06	0.73	0
Korea	1.12	29.1	48	24,699	1.12	6.1	36.50	10.09	27.67	0.43	0
Mexico	2.17	21.3	36	13,193	2.17	5.7	51.30	10.85	29.40	0.51	0
Netherland	1.72	28.9	12	38,173	1.72	9.7	5.60	N/A	29.04	N/A	0
New Zealand	2.01	28.0	29	23,968	2.01	9.3	16.60	25.30	33.73	0.60	1
Norway	1.9	27.7	75.3	52,079	1.9	8.6	15.40	20.78	28.33	0.42	0
Poland	1.27	25.8	4	14,342	1.27	6.2	25.60	18.22	34.25	0.37	0
Portugal	1.36	27.4	39	20,886	1.36	9.9	22.90	15.83	28.00	0.45	0
Spain	1.38	29.3	23	29,145	1.38	8.4	21.40	N/A	30.88	0.53	0
Sweden	1.85	28.7	14	34,903	1.85	9.1	16.20	22.10	29.55	0.49	1
Switzerland	1.44	29.5	15	41,107	1.44	10.8	30.80	11.84	23.89	0.60	0
Turkey[o]	2.17	26.7[p]	27	45,640	2.17	5.8	22.00		36.73	N/A	0
United Kingdom	1.84	29.8	26	34,298	1.84	8.5	11.40	18.07	27.62	0.61	0

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SUPPLEMENTAL TABLE 1

Continued.

Country	Total fertility rate[c]	Mean maternal age at first childbirth (2005 data)[d]	Level of urbanization[e]	GNI per capita (USD2006)[e]	Total infant mortality rate[c]	Health expenditure/ GDP[c]	Out-of-pocket expenditure/ total health expenditure[c]	Proxy for implantation rate (% babies/ embryos tranferred in fresh cycles)	ART clinical pregnancy rate (clinical pregancies/ initiated fresh ART cycle)	Percentage of ART patients aged $\geq$35 y	Policy linking ART funding to SET. 1 = policy exists[b]
United States	2.1	25.1	45	45,610	2.1	15.5	12.30	18.38	35.00	0.58	0
U.S. states (mandates)[q,s]	1.91	25.1	75	53,368	1.91	13.5	12.30	18.40	35.44	N/A	0
U.S. states (nonmandated)[r,s]	1.96	25.1	43	41,752	1.96	13.7	12.30	18.40	38.89	N/A	0
Brazil	2.3	26.4[p]	85	8,810	2.3	7.5	63.80	10.46	28.50	0.57	0
Argentina	1.7	27.5[p]	88	11,740	1.7	10.1	43.80	12.12	23.91	0.58	0

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[b] Published estimates, policies and clinic surveys.
[c] OECD Health Statistics: www.oecd-ilibrary.org/social-issues-migration-health/data/oecd-health-statistics_health-data-en. OECD Factbook 2010: Economic, Environmental and Social Statistics - ISBN 92-64-08356-1 - © OECD 2010.
[d] United Nations Economic Commission for Europe Statistical Division Database: http://w3.unece.org/pxweb/.
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[l] Centers for Disease Control and Prevention, American Society of Reproductive Medicine, Society of Assisted Reproductive Technologies. U.S. Department of Health and Human Services 2006 assisted reproductive technology success rate: national summary and fertility clinic reports. Atlanta: CDC, 2008.
[m] Age distribution for Belgium based on 2005 data.
[n] 2008 ART embryo practice data used for Japan.
[o] 2007 embryo transfer practices used for Turkey.
[p] Values imputed by regressing the known values for the variable.
[q] U.S. states with comprehensive ART insurance mandates (Connecticut, Massachusetts, New Jersey). Elective SET reported.
[r] U.S. states with no fertility treatment insurance mandates (Michigan, Oregon, Washington). Elective SET reported.
[s] Specific data sources for U.S. states: U.S. averages used for: physicians per capita,[c] mean age of women at first childbirth,[d] out-of-pocket expenditure/total health expenditure,[c] annual disposable income,[a] and gross cost of an ART cycle[b]; U.S. state-based data sources used for:
Population estimates: U.S. Census: U.S. Census Bureau, Population Division, Intercensal Estimates of the Resident Population by Sex and Age 2000–2010.
ART treatment data including implantation rate, clinical pregnancy rate, and age distribution.[l]
Estimates of out-of-pockets based on e-mail survey to CDC-registered clinics in the six representative states with and without comprehensive insurance mandates for ART.
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