contribution of donor ART to total births increased with maternal age, and the technique accounted for more births than did autologous ART among women in the 2 oldest maternal age groups. Gestational carrier use also increased with maternal age, accounting for 20.4% (95% CI, 18.7%-22.2%) of births to women 50 years or older.

Discussion | The contribution of ART to live births was clustered among older maternal age groups, and much of this disproportionate usage was driven by donor ART. Births following autologous ART among older maternal age groups predominately used frozen embryos, as expected given the low success rates for autologous ART using fresh embryos among older women.[2] Given the association between advanced maternal age and many obstetric complications,[6] the role of ART in enabling births to older women merits public health consideration. The analysis may underestimate the true contribution of ART to total births because some clinics do not report to NASS and some births following ART by non-US residents may have occurred in the United States. Additional limitations include potential data entry errors and lack of information on the year in which thawed embryos or oocytes were frozen. Despite these limitations, the analysis used the best data available and may be useful to patients, clinicians, and organizations (including medical societies as well as state and federal agencies) interested in improving maternal and infant health and the practice of ART.

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In Vitro Fertilization Insurance Coverage and Chances of a Live Birth

Because in vitro fertilization (IVF) is expensive and often cost-prohibitive, some states mandate IVF insurance coverage.[1] Previous analyses of aggregate, state-level data suggest these mandates are associated with increased IVF utilization but lower live birth rates per IVF cycle.[2] These analyses did not account for important confounders or for the fact that women may require multiple IVF cycles to achieve a live birth.[3] This study compared the cumulative probability of live birth among women with and without IVF insurance coverage at the Fertility and Reproductive Medicine Center at Washington University—a center located near the border between Illinois, which mandates IVF coverage, and Missouri, which does not.[4]

Methods | This retrospective study and waiver of consent was approved by the Washington University Human Research Protection Office. Women initiating IVF from 2001 through 2010 were included and observed through 2014. Women residing more than 160 kilometers from the center or using donor oocytes or gestational carriers were excluded. Data extracted from medical and billing records are listed in **Table 1**. The primary outcome was cumulative probability of live birth according to IVF insurance status over 4 IVF cycles, calculated as a function of live birth rates and return probabilities. Four IVF cycles are covered by the Illinois mandate. Cycles were defined as controlled ovarian hyperstimulation started with intent of fresh or subsequent frozen embryo transfer. To account for differences in patient characteristics by insurance status, logistic regression was used to estimate risk-adjusted live birth probabilities after the first, second, third, and fourth cycles and risk-adjusted return probabilities if a woman was unsuccessful after a given cycle. Covariates included IVF cycle number, interactions between insurance status and IVF cycle number, age at oocyte retrieval, race, prior live birth, income, fresh vs frozen embryo transfer, and linear time trend. For fresh embryo transfers, covariates also included antral follicle count, total amount of gonadotropin used, peak estradiol, and number of oocytes retrieved. Return probabilities included the above covariates, cycle cancellation, and the woman's distance from the clinic by residence zip code. Women were defined as returning if they did so within 365 days of an unsuccessful cycle. Standard errors were bootstrapped using 1000 replications.[5] Two-sided tests of significance were conducted with a threshold significance level of .05. Analyses were performed in STATA (StataCorp), version 13.1.

Table 1. Characteristics of Women at First Cycle Initiating IVF From 2001 Through 2010[a]

	Self-pay (n = 697)	IVF Insurance Coverage (n = 875)
Age, No. (%), y		
<35	369 (53)	569 (65)[b]
35 to 37	167 (24)	175 (20)
38 to 40	63 (9)	70 (8)
>40	98 (14)	61 (7)[b]
Race, No. (%)[c]		
White	516 (74)	665 (76)
Prior live birth, No. (%)	160 (23)	228 (26)
AFC, mean (SD)	15.6 (9.9)	16.8 (10.4)[d]
Total gonadotropin dose, mean (SD), IU	2389.5 (1062.8)	2279.5 (1127.9)[d]
Peak estradiol, mean (SD), pg/mL	1931.2 (1039.5)	2026.2 (945.6)
Oocytes retrieved, mean (SD)	11.8 (5.9)	12.1 (6.5)
ICSI, No. (%)	209 (30)	262 (30)
Assisted hatching, No. (%)	272 (39)	306 (35)
Embryos transferred, mean (SD)	2.27 (0.90)	2.18 (0.80)[d]
Covered by state IVF insurance mandate, No. (%)	NA	359 (40)
Infertility diagnosis, No. (%)		
Male factor	216 (31)	289 (33)
Endometriosis	125 (18)	140 (16)
Ovulation disorder	91 (13)	149 (17)
Tubal factor	28 (4)	26 (3)
Unexplained infertility	146 (21)	158 (18)
Average income, mean (SD), US $ thousands[e]	78.6 (38.2)	64.9 (24.0)[b]
Distance to clinics, median (10th-90th percentile), km[e]	23.9 (5.6-106.0)	35.6 (13.6-140.4)[b]

Abbreviations: AFC, antral follicle count; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; NA, not applicable.

[a] The *t* tests were conducted for the equality of the means between the insured and not insured.

[b] $P < .01$.

[c] Race is known to be associated with IVF outcomes and was self-reported.

[d] $P < .05$.

[e] Determined by patient zip code.

Table 2. IVF Cycle Outcomes by Insurance Status Among Women

	Cycle Number			
	1	2	3	4
No. of Women Undergoing Treatment in Cycle				
Insured	875	369	135	42
Self-pay	697	229	73	20
No. of Women With Live Birth in Cycle				
Insured	350	114	39	9
Self-pay	253	71	20	8
Proportion of Women With Live Birth in Cycle				
Insured	0.400	0.309	0.289	0.214
Self-pay	0.362	0.310	0.274	0.400
Difference (95% CI)	0.037 (−0.011 to 0.085)	−0.001 (−0.078 to 0.075)	0.015 (−0.115 to 0.145)	−0.186 (−0.427 to 0.056)
Proportion of Women Without Live Birth in Cycle Who Returned for Another Cycle				
Insured	NA	0.703	0.529	0.438
Self-pay	NA	0.516	0.462	0.377
Difference (95% CI)	NA	0.187 (0.127 to 0.248)[a]	0.067 (−0.032 to 0.167)	0.060 (−0.107 to 0.228)
Cumulative Live Birth Probability After Cycle No. (Unadjusted)				
Insured	0.400	0.531	0.575	0.585
Self-pay	0.363	0.465	0.493	0.505
Difference (95% CI)	0.037 (−0.011 to 0.085)	0.066 (0.016 to 0.117)[b]	0.082 (0.031 to 0.117)[a]	0.081 (0.030 to 0.131)[a]
Cumulative Live Birth Probability After Cycle No. (Risk-Adjusted)[c]				
Insured	0.388	0.517	0.557	0.566
Self-pay	0.379	0.480	0.503	0.512
Difference (95% CI)	0.010 (−0.039 to 0.055)	0.037 (−0.010 to 0.083)	0.053 (0.006 to 0.098)[b]	0.054 (0.008 to 0.099)[b]

Abbreviations: IVF, in vitro fertilization; NA, not applicable.

[a] Denotes difference between insured and self-pay was significant at .01 level.

[b] Denotes difference between insured and self-pay was significant at .05 level.

[c] Risk-adjusted cumulative live birth rate was calculated using estimated logit models for live birth (*c* statistic = 0.687) and return after failure (*c* statistic = 0.681).

Results | Of the 1572 women in the sample (230 excluded), 875 (55.7%) had IVF insurance coverage (40% mandated, 60% nonmandated) and 697 (44.3%) were self-pay. The 2 groups did not differ medically, but patients with coverage were younger (Table 1). IVF coverage status was not associated with probability of live birth in individual cycles (**Table 2**). However, the proportion returning for a second cycle if unsuccessful in the first cycle was 0.703 among women with coverage compared with 0.516 among self-paying women (difference, 0.187 [95% CI, 0.127-0.248]; $P < .001$) (Table 2). The mean cumulative live birth probability after 4 cycles for women with coverage 0.585, was significantly higher than that for self-paying women, 0.505 (difference, 0.081 [95% CI, 0.030-0.131]; $P = .001$). The difference in cumulative live birth rates adjusting for patient risk factors between insured and self-pay patients after 4 cycles narrowed to 0.054, but was still significant (95% CI, 0.008-0.099; $P = .01$).

Discussion | Women with insurance coverage for IVF were more likely to attempt IVF again, and they had a higher cumulative probability of live birth than women who self-paid for IVF. This study was limited because the data were obtained from 1 center and the findings may not apply to other centers. Also, out-of-pocket costs and information about women who may have returned elsewhere after a failed cycle were not available, but access to patient-level data allowed control for other important confounders. These findings demonstrate legislation mandating IVF insurance coverage may improve the delivery and outcomes of fertility treatments.

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COMMENT & RESPONSE

Inpatient Palliative Care After Hematopoietic Stem Cell Transplantation

To the Editor Dr El-Jawahri and colleagues[1] assessed the effect of inpatient palliative care on patient- and caregiver-reported outcomes after hematopoietic stem cell transplantation (HCT). They reported that the intervention group had better quality-of-life scores and secondary outcomes such as depression and anxiety.

The study protocol states that psychopharmacological agents such as benzodiazepines, atypical antipsychotics, and antidepressants could be prescribed to the intervention group for common symptoms such as nausea, insomnia, and depression. The use of these medications is a confounder that can directly reduce patient-reported anxiety and depression symptoms. Furthermore, antidepressants are generally prescribed for durations of 4 to 8 weeks.[2] Continual use of these medications could have contributed to the significant difference in Patient Health Questionnaire 9 scores among both study groups at 3 months after HCT, which was not present at 2 weeks. A study by Prieto and colleagues[3] analyzing Hospital Anxiety and Depression Scale (HADS) scores among patients undergoing HCT excluded individuals taking psychopharmacological agents because they were considered to affect outcomes. The number of patients prescribed psychopharmacological agents and their dose and duration should have been mentioned in the article. It also would have been appropriate to analyze the HADS scores of participants taking psychopharmacological agents separately to assess the extent to which physical symptom control affected study outcomes without the confounding effects of these medications.

The authors stated that the lack of blinding in the study "may have diluted the study findings" by improving the transplant team's care of the control group. However, the study reported a significant increase in HADS anxiety scores from baseline to 2 weeks in the control group, which conflicts with current literature. Previous studies found a decrease in HADS anxiety scores from baseline in patients after HCT despite increasing symptom burden.[3,4] Anxiety is often influenced by the patient's perception of events. The discrepancy