

OBSTETRICS

Medical cost savings associated with 17 alpha-hydroxyprogesterone caproate

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OBJECTIVE: This study was undertaken to assess the impact of 17 alpha hydroxyprogesterone caproate treatment on future medical costs for expectant mothers with a prior spontaneous preterm birth.

STUDY DESIGN: Data on the costs of preterm birth were combined with published data on the effectiveness of 17 alpha hydroxyprogesterone caproate to produce estimates of the effect of treatment on expected future direct medical costs. These estimates were compared with an estimate of the cost of a typical 17 alpha hydroxyprogesterone caproate treatment regimen to estimate the net savings per treated woman.

RESULTS: Treatment is estimated to reduce initial neonatal hospitalization costs by \$3800 per woman treated with 17 alpha hydroxypro-

gesterone caproate. Expected lifetime medical costs (discounted) of treated infants are estimated to decline \$15,900.

CONCLUSIONS: Treating expectant mothers with a prior spontaneous preterm birth with 17 alpha hydroxyprogesterone caproate generates future medical cost savings that substantially exceed the cost of treatment. If this population were universally treated with 17 alpha hydroxyprogesterone caproate, discounted lifetime medical costs of their offspring could be reduced by more than \$2.0 billion annually.

Key words: 17 alpha hydroxyprogesterone caproate, low birthweight, neonatal medical costs, preterm birth

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Reducing rates of preterm birth (PTB) could substantially reduce medical expenditures in the United States. In 2003, PTB occurred in approx-

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★ EDITORS' CHOICE ★

imately 12.3% of births nationwide, affecting nearly half a million infants.¹ Although mortality rates of preterm infants have declined over time, morbidity of surviving infants has increased because of survival of more seriously ill infants,² increasing the mean neonatal costs for surviving preterm infants.³⁻⁵ Mean neonatal costs were estimated to be \$17,300 greater (in 2004 dollars) for preterm infants relative to term infants, suggesting additional neonatal costs of preterm infants account for more than \$8.6 billion of annual medical spending in the United States.⁶

Recently published evidence that is based on randomized control trials indicates that 17 alpha hydroxyprogesterone caproate (17P) is effective in the prevention of recurrent spontaneous PTB.⁷⁻⁹ Prior spontaneous preterm birth (PSPTB) is one of the strongest risk factors for preterm birth,¹⁰ and the largest randomized trial of 17P tested was specifically on this population.⁷ On the basis of these findings, the American College of Obstetricians and Gynecologists has stated that a history

of PSPTB is an appropriate indication for using 17P to prevent PTB.¹¹ Petrini et al¹² estimate that approximately 133,000 expectant mothers have a history of PSPTB and are eligible for 17P each year, and treatment of this population could prevent 10,000 PTBs annually.

The purpose of our article is to assess the economic impact of 17P treatment for expectant mothers with PSPTB in terms of subsequent medical costs.

METHODS

Data sources

Medical costs associated with PTB. We identified 6 studies estimating the medical costs associated with PTB. These were identified via a MEDLINE search using the search terms "health care costs" and "prematurity," with additional studies identified from references. Studies consisting of non-US data were excluded. Also excluded were studies that did not provide or allow for computation of the incremental medical costs associated with preterm vs normal term deliveries. Six studies meeting our criteria were identified and are described briefly in Table 1.^{2-4,13}



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TABLE 1
Studies estimating medical costs associated with gestational age and/or birthweight outcomes

Study	Sample	Birth categories	Costs considered	Covariate adjustment	Nonsurvivors
Phibbs and Schmitt ⁶	California hospital births, 1998-2000, gestational age 24-37 wks	Gestational age (14 categories)	Neonatal hospital costs through discharge	None	Included
Gilbert et al ³	California hospital births, 1996, gestational age 25-38 wks	Gestational age (14 categories) Birthweight (11 categories)	Maternal and neonatal hospital costs through discharge	None	Omitted
St. John et al ⁴	Infants born at single Alabama hospital, 1989-1992, excluding transfers	Gestational age (19 categories)	Neonatal hospital costs and physician fees through discharge	Infant race and sex; length of stay	Included*
Schmitt et al ⁵	California hospital births, 2000	Birthweight (9 categories)	Prenatal, neonatal and maternal hospital costs through discharge	None	Included
Lewit et al ¹³	Data drawn from numerous sources (see study for details), with authors calculations intended to be representative of all US births in 1988	Birthweight (2 categories)	All infant medical costs through age 1 y	Infant race/ethnicity and sex; family income; mother's age and education; region and urban/rural indicators	Omitted
EPA-COI ^{2†}	Cost estimates derived from results in Lewit et al ¹³ (see study for details), and are therefore representative of US population in 1988	Birthweight (2 categories)	All infant medical costs through age 15 All infant medical costs through age 75	Infant race/ethnicity and sex; family income; mother's age and education; region and urban/rural indicators	Omitted

* To account for differences in how the St. John et al study treated nonsurviving infants, we combined the survivor/nonsurvivor cost estimates by taking the weighted mean across the 2 groups, with weights determined by their estimate of the proportion of survivors in each gestational age category (reported in their Table 2).

† The EPA Cost of Illness Handbook² imputes long-term incremental medical costs associated with low birthweight (LBW) (birthweight <2500 g) from estimates reported in Lewit et al¹³ and therefore does not represent an independent study in itself. Two particular imputations deserve mention. First, Lewit et al¹³ estimate incremental hospitalization costs (including medical fees associated with hospitalization) for LBW children through age 10 y. The EPA generated comparable estimates over years 11-75 of life assuming the incremental hospitalization costs associated with the age 6-10 y cohort reflect the incremental hospitalization costs of LBW in succeeding years. Second, incremental hospitalization-related costs systematically understate the total incremental medical costs of LBW by ignoring nonhospital medical care (eg, outpatient visits, pharmaceutical use, therapeutic services). The EPA addresses this bias using the inpatient/outpatient cost ratio for asthmatic children as an estimate for the inpatient/outpatient cost ratio of LBW children. Although these imputations are reasonable, they present additional uncertainty in the EPA-COI² estimates.

The 6 studies identified vary in a number of important respects. First, the studies vary in their categorization of outcomes (birthweight vs gestational age, number of categories). Second, the studies vary in the medical costs considered and their treatment of nonsurvivors. Third, the studies vary in the extent that cost estimates are adjusted for covariates. Fourth, the studies vary in terms of the time spans over which preterm costs were estimated. All cost estimates were converted to 2004 dollars by using the Consumer Price Index for medical care services.¹⁴ The Environmental Protection Agency's Cost of Illness Handbook (EPA-COI)² provides the only com-

prehensive estimate of long-term medical costs, with the remaining studies primarily focuses on hospital costs through discharge. For long-term costs estimated in the EPA-COI Handbook,² we use the results discounting future costs at a 3% annual rate.

Effectiveness of 17P for preventing preterm delivery

Drawing on 2 recently published meta-analyses,^{8,9} we identified 7 randomized control trials (RCTs) examining the effect of 17P on women at risk for preterm

delivery.^{7,15-20} A MEDLINE search using the terms "hydroxyprogesterone" and "preterm birth" failed to find any additional RTCs examining the effect of 17P treatment published since 1990.

Of the identified studies, we use the results of Meis et al⁷ to provide our estimate of treatment effectiveness. This decision reflects a number of considerations. First, the study by Meis et al⁷ was conducted recently, whereas the others were conducted before 1985. Second, the study by Meis et al⁷ used a sample 3 to 15 times larger than the others. Most importantly, the selection criteria used across the studies varied, with only Meis

TABLE 2

Effect of progesterone treatments on high-risk pregnancy outcomes comparative estimates

Panel A: Gestational age outcomes

Study	Gestational age (wk)	Treatment group (proportion)	Control group (proportion)	Effect estimate OR [95% CI]
Meis et al ⁷	<32	0.114	0.196	0.53 [0.31-0.90]
	<35	0.206	0.307	0.58 [0.38-0.91]
	<37	0.363	0.549	0.47 [0.31-0.69]
Sanchez-Ramos et al ⁸ (pooled estimate)	<37	0.293	0.409	0.45 [0.35-0.66]

Panel B: Birthweight outcomes

Study	Birthweight (g)	Treatment group (proportion)	Control group (proportion)	Effect estimate OR [95% CI]
Meis et al ⁷	<1500	0.086	0.139	0.59 [0.32-1.08]
	<2500	0.272	0.411	0.54 [0.36-0.81]
Sanchez-Ramos et al ⁸ (pooled estimate)	<2500	0.203	0.284	0.50 [0.36-0.71]

et al⁷ specifically focusing on expectant mothers with PSPTB.

Questions have been raised about whether the treatment effect estimates in Meis et al⁷ are generalizable to the obstetric population at large given the high prevalence of PTB in the control group.⁹ To address this concern, Table 2 reports estimates of effect of 17P treatment from the study by Meis et al⁷ in terms of its effect on the odds-ratio for PTB. Compared with the pooled 17P effect estimated in the meta-analysis by Sanchez-Ramos et al,⁸

the Meis et al⁷ estimate is modestly smaller. Thus, the Meis et al⁷ treatment effect estimate appears consistent with other studies despite the unusually high prevalence of PTB in their control group.

Baseline risk of preterm delivery among women with prior PTB

Two studies were identified that estimate the distribution of birth outcomes among expectant mothers with PSPTB.^{12,21} We use the distribution of gestational age outcomes estimated by

Mercer et al²¹ because they provide a finer categorization of gestational age outcomes and are a somewhat more conservative estimate of the recurrent PTB rate than Petrini et al.¹² The Mercer data are sufficiently old that 17P treatment rates would be virtually zero. The estimated proportion of births in each gestational age category is presented for each study in Table 3, Panel A ("Baseline Proportion").

As some of our cost estimates are in terms of birthweight, the results of

TABLE 3

Predicted effect of 17P treatment on distribution of birth outcomes expectant mothers with prior PTB

Panel A: Gestational age outcomes

Study	Gestational age (wk)	Baseline proportion	Treatment proportion	Predicted difference	Conservative difference
Mercer et al ²¹	<32	0.051	0.028	-0.024	
	<35	0.134	0.083	-0.051	
	<37	0.217	0.115	-0.102	-0.056
Petrini et al ¹²	<37	0.225	0.120	-0.105	-0.062

Panel B: Birthweight outcomes

Study	Birthweight (g)	Baseline proportion	Treatment proportion	Predicted difference	Conservative difference
Mercer et al ²¹	<1500	0.049	0.029	-0.020	
	<2500	0.188	0.111	-0.077	-0.030

Note: "Baseline Proportion" reflects fraction of births in a particular gestational age/birthweight category to women with PPTB as estimated in the study indicated. "Treatment Proportion" is inferred by applying 17P treatment effect (odds-ratio) estimates from Meis et al⁷ to estimated proportion of births in each gestational age/birthweight category. "Predicted Difference" estimates the expected change in the proportion of births in each category resulting from 17P treatment. "Conservative Difference" estimates the expected change applying a conservative estimate of the 17P treatment effect, based on the upper bound of the 95% CI around the Meis et al⁷ estimate.

Mercer et al²¹ were used to infer a comparable distribution of birthweight outcomes for expectant mothers with PSPTB. We combined the estimates of Mercer et al²¹ with estimates for the distribution of birthweight outcomes over births of different gestational ages²² to estimate the proportion of expectant mothers with PSPTB delivering children less than 1500 g or less than 2500 g in birthweight. (Table 3, Panel B, "Baseline Proportion").

Data integration and cost savings analysis. Treatment effectiveness estimates from Meis et al⁷ were combined with estimates of the medical costs associated with preterm and term birth to generate estimates of the expected reduction in medical costs associated with 17P treatment for women with PSPTB. The cost of the treatment itself is calculated separately and excluded from these estimates.

Gestational age and birthweight categories were combined as necessary to match those reported in Meis et al.⁷ Cost estimates for these combined categories were generated by taking the weighted mean of cost estimates within the individual categories. For instance, Gilbert et al³ reports neonatal and maternal costs by single week of gestational age. To generate a cost estimate for the combined category "gestational age = 32-34 weeks," we calculated the weighted mean over the 3 single-week categories, with weights determined by the relative proportion of births in each of the single-week categories.

To calculate expected cost savings, the (odds ratio) treatment effect estimates from Meis et al⁷ were applied to the estimated distribution of births in different gestational age and birthweight categories (from Mercer et al²¹) to estimate the expected proportion in each category had 17P been administered. From this, we estimated the expected change in the proportion of births in each category, which were then applied to the cost estimates from the medical cost studies. The estimated change in medical costs (ΔC) associated with treatment was calculated as $\Delta C = \sum \Delta p_j C_j$, where subscript j identifies a particular gestational age or birthweight category, Δp_j is the estimated

change in the proportion of births in category j associated with 17P treatment, and C_j is the estimated medical costs associated with a birth in category j .

Three cost savings estimates were generated in this way. The first uses the finest categorization of gestational ages or birthweights available in calculating ΔC . The second calculates ΔC using only 2 gestational age or birthweight categories, with preterm defined as gestational age less than 37 weeks or birthweight less than 2500 g. The third estimate also uses the binary categories and uses a conservative treatment effect estimate, based on the upper bound of the 95% CI around the Meis et al⁷ treatment effect estimate.

Estimating cost of standard 17P treatment regimen. A standard 17P treatment regimen consists of 21 injections, typically administered by a registered nurse. The cost per injection therefore consists of the cost of drug plus the value of the nurse's time. The cost per dosage of 17P was obtained by telephoning 2 national pharmacies that supply 17P. The hourly value of nursing time was inferred from the national mean hourly wage of registered nurses in 2004.²³ We assume that each injection requires 15 minutes of nurse time, and that treated patients receive the full 21-injection regimen. The estimated cost of treatment per treated patient is therefore estimated as $21 \times (\text{drug cost per dosage} + \text{mean hourly registered nurse wage}/4)$. This is likely an overestimate of the expected treatment costs per treated patient because patients delivering before 37 weeks would not receive the full regimen of injections.

RESULTS

Table 3 reports the estimated change in the proportion of births in different gestational age and birthweight categories with 17P treatment ("Predicted Difference"). On the basis of the distribution of birth outcomes among women with PSPTB, 17P treatment of these women is predicted to reduce the incidence of births occurring at less than 37 weeks by more than 10 percentage points. Applying the conservative estimate of the 17P

effect, the incidence of births occurring at less than 37 weeks is reduced 5.6 percentage points ("Conservative Difference"). The results for birthweight are more modest. 17P treatment is estimated to reduce the incidence of birth weight less than 2500 g by 7.7 percentage points, falling to 3.0 percentage points by using the conservative treatment effect estimate.

Estimates of short-term medical cost savings from treating at-risk pregnancies with 17P, based on gestational age treatment effects, are shown in Table 4. Cost savings estimates ("Expected Savings") are presented as the expected reduction in medical costs per patient treated. Estimates vary depending on which of the cost studies are used and whether more detailed gestational age categories are used. By using 4 gestational age categories, the estimated cost savings ranged from \$2900 to \$3800. The estimated savings are more modest when 2 gestational age categories are used, ranging from \$1600 to \$2600. Our conservative estimates suggest savings in the range of \$900 to \$1400.

Table 5 reports estimates of medical cost savings when inferred from predicted changes in the distribution of birthweight outcomes. Cost estimates using detailed birthweight categories range from \$2300 to \$3900, declining to \$1600 to \$2900 when binary birthweight categories are used, and \$600 to \$1100 when the conservative treatment effect estimate is applied. Cost savings over the first year, based on the Lewit et al¹³ cost estimates, can only be estimated over the binary categories. We estimate medical cost savings of \$2700 over the first year of life, declining to \$1000 when the conservative treatment effect estimate is applied.

The final 2 columns of Table 5 report long-term cost savings estimates associated with 17P treatment based on EPA-COI² cost estimates. Again, these can only be calculated by using binary birthweight categories. We estimate that 17P treatment reduces (discounted) medical costs by \$7500 over the first 15 years of life, increasing to \$15,900 through age 75. Applying the conservative treatment effect estimate,

TABLE 4

Medical costs by gestational age and estimated savings from 17P treatment

	Cost estimate study included medical costs		
	Phibbs and Schmitt ⁶ Neonatal hospital costs	Gilbert et al ³ Maternal and neonatal hospital costs	St. John et al ⁴ Neonatal hospital costs and related fees
Panel A: Mean medical costs by gestational age			
<32 wks	\$138,300	\$105,400	\$92,200
32-34 wks	\$19,800	\$20,200	\$23,300
35-36 wks	\$4500	\$8900	\$6400
<37 wks	\$19,400	\$20,700	\$28,100
≥37 wks	\$2100	\$5300	\$2300
Panel B: Estimated savings per treated mother			
Estimate 1	\$3800	\$2900	\$2900
Estimate 2	\$1800	\$1600	\$2600
Conservative estimate	\$1000	\$900	\$1400

Note: Costs estimated through discharge. Cost estimates from the original studies were converted to 2004 dollars using Consumer Price Index for medical care services. "Estimate 1" estimates expected savings from treatment based on predicted change in proportion of births across 4 gestational age categories (<32, 32-34, 35-36, and ≥37 wks). "Estimate 2" estimates expected savings from treatment based on predicted change in proportion of births across 2 gestational age categories (<37 and ≥37 wks). "Conservative Estimate" replicates Estimate 2 applying conservative estimate of treatment effect.

the savings estimates decline to \$2900 and \$6100, respectively.

The cost of a typical 17P treatment regimen is relatively modest. Each drug dose costs \$10 or \$12.60 based on 2 national pharmacies we interviewed. The value of nursing time required to perform each injection is estimated as

mean hourly wage of registered nurses (\$26.06 in 2004) divided by 4, or \$6.52. By using the higher of the reported drug costs, the estimated cost per injection is \$19.12. Assuming treated patients receive all 21 injections, the estimated cost per treated patient is about \$400.

If all pregnant women with a PSPTB the United States were universally treated with 17P, the aggregate savings would be substantial. Petrini et al estimates that nearly 133,000 women are eligible for 17P treatment in a given year, based on the annual number of expectant mothers with PSPTB who receive

TABLE 5

Medical costs by birthweight and estimated savings from 17P treatment

	Cost estimate study and included medical costs				
	Schmitt et al ⁵ Prenatal, neonatal and maternal hospital costs*	Gilbert et al ³ Maternal and neonatal hospital costs*	Lewit et al. (1995) All infant medical costs to age 1 y	EPA-CO1 ² All infant medical costs to age 15 y	All infant medical costs to age 75 y
Panel A: Mean medical costs by birthweight					
<1500 g	\$152,800	\$88,900	—	—	—
1500-2500 g	\$22,500	\$16,300	—	—	—
<2500 g	\$43,000	\$25,600	\$39,300	\$96,500	\$205,200
≥2500 g	\$5200	\$5000	\$4400	—	—
Panel B: Estimated savings per treated mother					
Estimate 1	\$3900	\$2300	—	—	—
Estimate 2	\$2900	\$1600	\$2700	\$7500	\$15,900
Conservative estimate	\$1100	\$600	\$1000	\$2900	\$6100

Note: Cost estimates from the original studies were converted to 2004 dollars using Consumer Price Index for medical care services. EPA-CO1² only reports incremental medical costs associated with LBW status (<2500 g). EPA-CO1² cost estimates apply 3% discount rate to costs beyond the first year. "Estimate 1" estimates expected savings from treatment based on predicted change in proportion of births across 3 birthweight categories (<1500, 1500-2500, and ≥2500 g). "Estimate 2" estimates expected savings from treatment based on predicted change in proportion of births across 2 birthweight categories (<2500 and ≥2500 g). "Conservative Estimate" replicates Estimate 2 applying conservative estimate of treatment effect.

* Costs measured through discharge.

prenatal care within the first 4 months of pregnancy.¹² The annual cost of treating these women with 17P would be around \$53 million, assuming a full course of treatment for each woman. These up-front costs are offset by the expected future savings from reduced rates of PTB. On the basis of the cost savings estimates derived from the most recent studies, universal treatment of these women would reduce initial medical costs by more than \$505 million, for an annual net savings of \$452 million. Over the lifetime of affected infants, the estimated net annual savings exceeds \$2.0 billion.

COMMENT

Our analysis indicates that 17P treatment for expectant mothers with PSPTB generates future medical cost savings that substantially exceed the cost of treatment. A realistic estimate for the expected cost savings associated with initial hospitalization is \$3800 per treated patient, for a net savings of \$3400 per treated patient. Our most conservative estimate suggests mean savings in initial hospitalization costs of about \$600 per treated woman, representing net savings of \$200 over the cost of treatment. This estimate is conservative mainly because it uses a conservative estimate of the 17P treatment effect and is based on binary birthweight categories instead of more detailed gestational age categories. Gestational age appears to be a stronger predictor of medical costs than birthweight, and using less fine categories systematically biases estimates downward by ignoring the disproportionate effect of 17P in reducing more severe birth outcomes. There is also evidence that the medical costs associated with PTB have been increasing over time, as larger savings estimates resulted from using more recent estimates of preterm costs.

Expanding the window of time generates even larger estimates of expected savings. 17P treatment would reduce expected (discounted) medical costs of treated infants by \$7500 through age 15 and \$15,900 through age 75. As these estimates are based on binary birthweight categories, they likely represent underestimates. Nonetheless, even by using the

conservative estimate of the 17P treatment effect, expected lifetime savings are estimated at \$6100 per patient, exceeding the cost of treatment by \$5700. We measured direct medical costs only. The true cost savings to society is likely to be higher than our estimates.

Our study has 2 important limitations. First, we assume that the incremental costs associated with PTB reflect a causal relationship, ie, that reducing the incidence of PTB would reduce medical costs in the amount suggested by the incremental cost estimates. It is conceivable that some of the incremental costs are caused not by the low gestational age or birthweight of the infant, but that separate medical or environmental factors contribute to both the preterm outcome and higher subsequent medical costs. As a result, treatments that reduce PTB but leave the underlying causal mechanism intact will not have the anticipated effect on future medical costs.

Our second limitation has to do with the treatment of mortalities in the cost estimate studies. Although omitting the nonsurvivors could potentially bias our cost estimates, this would not appear to apply to the short-term cost estimates. Short-term savings estimates based on the St. John et al⁴ cost estimates are comparable to those based on Gilbert et al³ and Lewit et al.¹³ The most recent cost studies included nonsurvivors and produced somewhat larger savings estimates. We acknowledge, however, that omitting nonsurvivors likely increases estimates of the long-term incremental costs of low birthweight in the EPA-COI Handbook,² because fewer preterm infants will survive to any given age and nonsurvivors consume no medical care. A "pure" analysis of future medical costs would include the zero medical care consumption of nonsurvivors in calculating the incremental medical costs of low birthweight, reducing the long-term incremental cost estimates, and thus reducing our estimates of long-term savings from 17P treatment. Instead, our long-term savings estimates implicitly assume that life expectancy does not vary across preterm and term infants. We offer 3 comments on this. First, we would expect the potential bias identified above

to be at least partially offset by the competing bias from having estimated long-term savings based on binary birthweight categories. Second, the cost estimates in the EPA-COI² represent medical costs in 1988, which likely understate the current incremental costs of PTB. Third, if 17P treatments increase the life expectancy of treated infants, this strengthens rather than weakens arguments for widespread adoption of 17P treatment, even if persons surviving as a result of the treatment happen to consume medical care.

17P is just starting to be adopted into clinical practice. One of the important barriers to 17P adoption is lingering concern over the safety of 17P treatment.²⁴ Given the sad history of diethylstilbestrol (DES), obstetricians may harbor justifiable concerns regarding the safety of hormonal agents in pregnancy and the associated exposure to malpractice litigation. Although existing animal and clinical evidence suggests that 17P is safe,²⁵ 17P is not an FDA-approved drug for the prevention of PTB. Until approval is given for this indication, it is unlikely that 17P treatment will be widely adopted.

Some patients may be taught to administer their own injection, and thus the costs of 17P may decrease. Alternatively, if injection of 17P is bundled with a home visit nurse these administration costs may increase. Assuming that an hour of nursing time is needed for a home health visit and that the nurse travels up to 20 miles at 0.445 cents/hour, with the drug and nursing costs as stated previously, a course of 21 injections by a home health nurse comes to \$998.76. The annual cost of treating eligible women with home health injections would be \$133 million and the annual net savings would be \$372.4 million. Over the life time of affected infants, cost savings would be \$1.98 billion annually. Thus, even with home health administration of 17P, the costs of administration are outweighed by the substantial costs savings in neonatal care. Of note we have calculated the cost of home health administration of 17P and not the charges. Charges and costs may be very different and home health agencies may

charge more than the service costs to provide.

Medicaid and private insurers often do not cover progesterone supplementation treatments and women of modest means may find 17P treatment cost prohibitive. From a purely financial perspective, the failure of insurers to cover 17P for expectant mothers with PSPTB is difficult to understand. Because the insurers of pregnant women generally cover the infant after delivery, our results indicate these insurers could recognize substantial savings by covering 17P, even in the short term. The argument for Medicaid coverage of 17P treatments is even more compelling. First, the poor suffer particularly high rates of PTB,²⁶ suggesting that a larger fraction of PTBs could be avoided with 17P treatment in this population. Second, because they are poor, the financial barriers to paying for 17P treatment out-of-pocket are especially severe for the Medicaid population. The potential societal savings from Medicaid coverage of 17P are substantial.

Treating expectant mothers with a PSPTB with 17P generates future medical cost savings that substantially exceed the cost of treatment. If the eligible population were universally treated with 17P, discounted lifetime medical costs of their offspring could be reduced by more than \$2.0 billion annually. ■

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REFERENCES

1. Martin J, Hamilton B, Sutton P, Ventura S, Menacker F, Munson M. Births: final data for 2003. Hyattsville (MD): National Center for Health Statistics; 2005.

2. United States Environmental Protection Agency. The Cost of Illness Handbook., Available at <http://www.epa.gov/oppt/coi/toc.html>. Accessed on June 2005.

3. Gilbert WM, Nesbitt TS, Danielsen B. The cost of prematurity: quantification by gestational age and birth weight. *Obstet Gynecol* 2003;102:488-92.

4. St John EB, Nelson KG, Cliver SP, Bishnoi RR, Goldenberg RL. Cost of neonatal care according to gestational age at birth and survival status. *Am J Obstet Gynecol* 2000;182:170-5.

5. Schmitt SK, Sneed L, Phipps CS. Costs of newborn care in California: a population-based study. *Pediatrics* 2006;117:154-60.

6. Phipps C, Schmitt S. Estimates of the cost and length of stay changes that can be attributed to one-week increases in gestational age for premature infants. *Early Hum Dev* 2006;82:85-95.

7. Meis PJ, Klebanoff M, Thom E, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. *N Engl J Med* 2003;348:2379-85.

8. Sanchez-Ramos L, Kaunitz AM, Delke I. Progesterone agents to prevent preterm birth: a meta-analysis of randomized controlled trials. *Obstet Gynecol* 2005;105:273-9.

9. Dodd J, Crowther C, Cincotta R, Flenady V, Robinson J. Progesterone supplementation for preventing preterm birth: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand* 2005;84:526-33.

10. Goldenberg RL, Iams JD, Mercer BM, et al. What we have learned about the predictors of preterm birth. *Semin Perinatol* 2003;27:185-93.

11. ACOG committee on obstetric practice. Use of progesterone to reduce preterm birth. Washington (DC): American College of Obstetricians and Gynecologists; 2003.

12. Petriani J, Callaghan W, Klebanoff M, et al. Estimated effect of 17 alpha hydroxyprogesterone caproate on preterm birth in the United States. *Obstet Gynecol* 2005;105:267-72

13. Lewit E, Baker L, Corman H, Shiono P. The direct cost of low birth weight. *Future Child* 1995;5:35-56.

14. Dodd JM, Crowther CA, Cincotta R, Flenady V, Robinson JS. Progesterone supplementation for preventing preterm birth: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand* 2005;84:526-33.

15. Yemini M, Borenstein R, Drazzen E, et al. Prevention of premature labor by 17 alpha-hy-

droxyprogesterone caproate. *Am J Obstet Gynecol* 1985;151:574-7.

16. Johnson JW, Austin KL, Jones GS, Davis GH, King TM. Efficacy of 17alpha-hydroxyprogesterone caproate in the prevention of premature labor.[see comment]. *N Engl J Med* 1975;293:675-80.

17. Papiernik-Berkauer E. Etude en double aveugle d'un medicament prevenant la survenue prematuree de l'accouchement chez les femmes a risque eleve d'accouchement premature edition. Schering. *Serie IV* 1970;3:65-8.

18. LeVine L. Habitual abortion: a controlled study of progesterone therapy. *West J Surg Obstet Gynecol* 1964;72:30-6.

19. Hartikainen-Sorri AL, Kauppila A, Tuimala R. Inefficacy of 17 alpha-hydroxyprogesterone caproate in the prevention of prematurity in twin pregnancy. *Obstet Gynecol* 1980;56:692-5.

20. Hauth JC, Gilstrap LC 3rd, Brekken AL, Hauth JM. The effect of 17 alpha-hydroxyprogesterone caproate on pregnancy outcome in an active-duty military population. *Am J Obstet Gynecol* 1983;146:187-90.

21. Mercer BM, Goldenberg RL, Moawad AH, et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol* 1999;181:1216-21.

22. Doubilet PM, Benson CB, Nadel AS, Ringer SA. Improved birth weight table for neonates developed from gestations dated by early ultrasonography. *J Ultrasound Med* 1997;16:241-9.

23. United States Department of Labor Bureau of Labor Statistics. Occupational employment and wages (29-1111 registered Nurses), May 2004. Available at <http://www.bls.gov/oes/current/oes291111.htm>. Accessed on July 29, 2005.

24. Ness A, Burd I, Damus K, Dias T, Berghella V. Current progesterone use and attitudes among board certified MFM specialists in the United States. *Am J Obstet Gynecol* 2005;193:S58.

25. Reproductive toxicology center. Reprotox, March 2003. Available at www.reprotox.org. Accessed on June 7, 2005.

26. National Institute of Child Health and Human Development. Health Disparities Bridging the Gap, 2000. Available at: <http://www.nichd.nih.gov/strategicplan/disparities.pdf>. Accessed May 17, 2004.