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Understanding barriers to utilization of 17-hydroxyprogesterone caproate and other interventions to prevent preterm birth in Fresno County, California

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Abstract

Objective: Preterm birth is one of the leading causes of neonatal morbidity and mortality. A history of prior spontaneous preterm birth is a known risk factor for recurrent preterm birth. While 17-alpha-hydroxyprogesterone caproate (17P) has been found in some studies to reduce recurrent preterm birth by 34%, many women who could have benefited from its use did not receive this intervention. We sought to investigate the rate of and reasons for underutilization of 17P in Fresno County, California, where the preterm birth rate trend from 2017 and recent 2020 data showed a significantly higher rate at 10.1% and 9.8% respectively, when compared to the state average of 8.6% and 8.8% respectively.

Methods: We conducted a retrospective chart review of patients who delivered at Community Regional Medical Center in Fresno from January to December 2016, and surveys of providers and patients, to help identify barriers to 17P utilization.

Results: After controlling for age, body mass index, interpregnancy interval, and race/ethnicity, we determined that women who had private insurance were 3 times more likely to have received 17P compared to women with public insurance (adjusted odds ratio 2.97, 95% CI: 1.6–6.51, p<.001). We also found that only 23.3% of patients eligible for 17P actually received this intervention. The surveys identified difficulty with completing the insurance approval process and receiving the treatment within the clinically recommended timeline as primary barriers to 17P utilization.

Conclusion: This study confirmed that 17P intervention for prevention of recurrent preterm birth was underutilized and disproportionately affected patients with inadequate prenatal care and those who had public insurance.

Keywords: Preterm birth, prevention, intervention barriers, 17-OHP.

Özet: Fresno County, Kaliforniya'da preterm doğumu önlemek için 17-hidroksiprogesteron kaproat ve diğer girişimlerden faydalanmanın önündeki engelleri anlamak

Amaç: Preterm doğum, neonatal morbidite ve mortalitenin önde gelen sebeplerinden biridir. Spontan preterm doğum geçmişi, rekürran preterm doğum için bilinen bir risk faktörüdür. Bazı çalışmalarda 17-alfa-hidroksiprogesteron kaproatın (17P) rekürran preterm doğumu %34 azalttığı bulunsa da, kullanımından faydalanamamış birçok kadına bu girişim uygulanmamıştır. Kalifroniya'daki Fresno County'deki preterm doğum oranı ile ilgili 2017 yılındaki eğilimi ve yeni 2020 yılı verileri (sırasıyla %10.1 ve %9.8), eyaletin aynı yıllar için kaydedilen sırasıyla %8.6 ve %8.8'lik verileri ile karşılaştırıldığında anlamlı bir şekilde daha yüksektir. Bu nedenle Fresno County'de, 17P'nin az kullanımının oranlarını ve amaçlarını araştırmayı amaçladık.

Yöntem: 17P kullanımına yönelik engelleri tespit etmeye yardımcı olması amacıyla 2016 Ocak – Aralık ayları arasında Fresno'daki Community Regional Medical Center'da doğum yapan hastaların çizelgelerini retrospektif olarak inceledik ve hizmet sağlayıcılar ile hastaların katıldığı anketler yaptık.

Bulgular: Yaş, vücut kitle indeksi, gebelikler arası aralık ve ırk/ etnik köken yönünden kontrol ettikten sonra, özel sigortası olan kadınların devlet sigortası olanlara kıyasla 3 kat daha fazla 17P aldıklarını belirledik (düzeltilmiş olasılık oranı 2.97, %95 GA: 1.6–6.51, p<.001). Ayrıca, 17P'ye uygun olan hastaların yalnızca %23.3'üne bu girişimin uygulandığını bulduk. Anketler, sigorta onay sürecini tamamlamanın ve klinik olarak tavsiye edilen süre içinde tedavi almanın zorluğunun 17P kullanımının önündeki ana engeller olduğunu ortaya koymuştur.

Sonuç: Çalışmamız, rekürran preterm doğumun önlenmesi için 17P girişiminin yetersiz şekilde kullanıldığını ve bu durumun eksik prenatal bakım alan ve devlet sigortası olan hastaları orantısız şekilde etkilediğini doğrulamıştır.

Anahtar sözcükler: Preterm doğum, önleme, girişim engelleri, 17-OHP.

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Introduction

Preterm birth, defined as delivery before 37 weeks gestation, is among the leading causes of neonatal morbidity and mortality.[1] Approximately, 1 in 10 babies are born preterm in the United States each year with annual estimated costs of $26.2 billion as was last reported in 2007, that included medical and non-medical costs.[2] The national preterm birth rate increased from 9.57% in 2014 to 10.02% in 2018.[3,4] According to the 2020 birth statistics data, in Fresno County, California, the preterm birth rate has been significantly higher at 9.8% compared to the state average of 8.8%.[5]

Risk factors for preterm birth include prior spontaneous preterm birth, multiple gestations, assisted reproductive techniques, and short cervical length.[6] African American women have nearly double the risk of having a preterm birth, contributory factors being racial discrimination and systemic inequality.[7] Other risk factors include maternal infections, anemia, hypertension, diabetes, short inter-pregnancy interval, vaginal bleeding, smoking, drug abuse, young maternal age, fetal and placental abnormalities, and psychosocial stressors.[6] Despite these identifiable risk factors, numerous barriers limit patients' access to early recognition, treatments and interventions. These barriers include but are not limited to inadequate prenatal care, gaps in communication between providers and patients, systemic racism and socio-cultural barriers that inhibit women from seeking care.[8]

Progesterone has long been known to have an inhibitory effect on uterine contractility and is thought to play a key role in the protection of pregnancy until term gestation. In 2003, the results of a multicenter placebo controlled randomized trial published by Meis et al., reported a 34 % reduction of recurrent preterm birth with weekly 17P injections in women with a history of prior spontaneous preterm birth (SPTB).[9] Based on these findings, the Society for Maternal-Fetal Medicine (SMFM) and American Congress of Obstetrics and Gynecology (ACOG) endorsed and recommended the use of 17P for prevention of recurrent preterm birth in women with a singleton gestation with a prior obstetrical history of spontaneous preterm birth.[10]

Subsequently, after the completion of our study, there has been a recent mixed evidence and controversy regarding the effectiveness of 17P based on the PROLONG study, published in 2019. In response to the PROLONG study results and the FDA decision, the SMFM issued a statement in support of continued use of 17P for the high risk patient population following an informed shared decision making between the provider and patients. The ACOG Practice Advisory has also endorsed the SMFM response.[11–13] In addition, a recent SMFM statement issued in March 2021, supported and recommended the use of 17P in women with a singleton gestation and a history of prior SPTB between 20 and 36 6/7 weeks of gestation in response to the published results of "Evaluating Progestogens for Preventing Preterm birth International Collaborative (EPPPIC): meta-analysis of individual participant data from randomized controlled trials".[14,15]

In Fresno County, California, as elsewhere, persistent racial health disparities exist with the highest preterm birth rate reported in African Americans (11.9%) and the lowest in the White population (7.7%). Moreover, while only 5.6% of infants born in Fresno County are African American, they represent 25.3% of infant deaths.[16] Although the specific reason for the higher rate of preterm delivery among African Americans in Fresno County is unknown, underutilization of 17P intervention for women with a history of preterm birth may play a role.[17] Previous research has shown that less than half of eligible women actually received the intervention.[18] Barriers can exist at multiple levels of care that include system barriers, provider-related barriers, and patient-level barriers. Some of these barriers include lack of access to early prenatal care, provider/patient's lack of knowledge, administration and patient-related costs, ability for compounding, time and appointment commitments, and potential adverse reactions to the medication.[19,20] In addition, prenatal care is now being offered by a variety of medical personnel, some of whom may not be aware of available interventions.[18,21]

Due to the significantly increased rate of preterm birth in Fresno County, we sought to investigate 17P utilization and understand the barriers to underutilization of 17P among eligible women. In addition, we studied the use of other evidence-based interventions including cerclage for cervical incompetence and vaginal progesterone for short cervix. Specifically, our goals were to: (1) understand the number of women who were eligible, were offered, and received 17P and other interventions and (2) understand provider, patient and system level barriers to accessing these treatments.

Methods

We conducted a retrospective chart review of patients who gave birth at the medical center included for our study from January to December 2016. The medical center studied is one of the largest Medi-Cal obstetrical providers in the county, with approximately 5000 deliveries each year.

The data was abstracted from patient's electronic medical records (EMR). Due to the discrepancies and limitations of EMR documentation of diagnosis codes referring to prior preterm birth history, our initial screening and review included all those with a prior preterm delivery diagnosis code, and current preterm delivery diagnosis code. This was done to ensure we did not miss patients in the category of prior preterm birth. Therefore, a total of 1294 patient's charts that were initially identified, screened and reviewed included prior and current preterm delivery diagnosis codes.

The detailed retrospective chart review and data analysis included all singleton pregnancies eligible for 17P based on history of prior spontaneous preterm birth following spontaneous preterm labor and/or history of premature preterm rupture of membranes resulting in preterm delivery prior to 37 weeks gestation.

Exclusion criteria applied to the sample of medical records involved medically indicated preterm births, multiple gestations, and fetal anomalies. Seven charts were also excluded upon review, one due to lack of 17P documentation and six others due to absence of current or previous preterm birth.

The detailed data abstraction from the electronic medical records included demographic characteristics (maternal age, race/ethnicity, insurance provider), clinical characteristics (body mass index [BMI], interpregnancy interval, presence of short cervix), prenatal care details (prenatal care initiation; receipt of 17P, vaginal progesterone, antibiotics, and/or cerclage), and birth outcomes (gestational age [GA] at delivery, infant birth weight and Apgar scores).

In addition, in order to assess operational and structural barriers that prevent eligible women from receiving 17P and other evidence-based interventions, patient and provider surveys were conducted. Fifteen patients who delivered preterm during the study period were randomly selected. These women were interviewed over the telephone by a study staff member using a scripted questionnaire.

Provider surveys were administered to prenatal care providers, that included physicians, licensed vocational nurses, medical assistants, nurse practitioners, and physician assistants, who were responsible for the majority of deliveries at the medical center included in our study. The provider survey comprised of questions about screening for preterm birth risk and knowledge of available interventions and the process for implementation of the prescribed interventions.

Participation in the survey component of the study was completely voluntary, with assurance that all responses would be anonymous and that there would be no impact on current/future health care nor employment. Forty-one survey responses were received.

The surveys were created and screened by the research team workgroup that included obstetrical providers, a perinatologist, public health nurse and maternal child health research investigators. The survey questionnaire was constructed and modified from other standardized surveys used across the country in similar research about 17P or other preterm birth interventions.[22,23] Data entry was done through Qualtrics and all surveys were analyzed using STATA (StataCorp LLC, College Station, TX, USA) and SPSS (IBM Corp., Armonk, NY, USA).

Multivariate models were used to explore associations between maternal characteristics and 17P utilization. Maternal characteristics were analyzed using chi-square to identify differences between those that received the intervention and those that did not. In addition, multiple regression was used to obtain adjusted odds ratios for the mothers that received 17P and their preterm birth outcomes.

Results

Out of the total 1294 women included in our chart review, 599 (46.3%) had a history of preterm delivery, and 695 (53.7%) had a current preterm delivery that occurred during the study period due to the EMR documentation discrepancies in the diagnosis codes. Among the sample of patients with history of previous preterm delivery, 378 (63.1%) had a prior spontaneous preterm birth and met the eligibility criteria for the 17P intervention. Maternal characteristics of women who had a previous spontaneous preterm birth were compared by the receipt of the 17P intervention. As summarized in

Table 1. The association between the characteristics of mothers with history of spontaneous PTD (S-PTD) and 17P intervention.

	All prior S-PTD n=378	Intervention received n=88 (23.3%)		Chi-square test of independence			Intervention not received n= 290	
Maternal characteristics	**n**	**n**	**%**	**n***	**Chi**	**p**	**n**	**%**
Maternal age				378	0.082	0.774		
<35 years	334	77	23.1				257	77.0
35+ years	44	11	25				33	75.0
BMI				338	0.028	0.867		
<35 BMI	274	70	25.6				204	74.5
35+ BMI	64	17	26.6				47	73.4
Bilinmiyor	40	1	2.5				39	97.5
Short IPI‡				348	6.496	0.011		
<18 months	164	29	17.7				135	82.3
18+ months	184	54	29.4				130	70.7
Unknown	30	5	16.7				25	83.3
Maternal race/Ethnicity				370	7.003	0.072		
AIAN	3	0	0				3	100.0
Asian	49	11	22.5				38	77.6
Black/AA	49	6	12.2				43	87.8
Hispanic or Latina	216	49	22.7				167	77.3
Native Hawaiian / PI	3	2	66.7				1	33.3
White	56	19	33.9				37	66.1
Unknown	2	1	50				1	50.0
Insurance payer status‡				366	13.404	0.0002		
Public	321	64	19.9				257	80.1
Private	45	20	44.4				25	55.6
Out of Pocket	12	4	33.3				8	66.7
Prenatal care received†				368	6.297	0.012		
Yes	349	88	25.2				261	74.8
No	19	0	0				19	100.0
Unknown	10	0	0				10	100.0
Prenatal care initiation‡				223	10.973	0.004		
First trimester	231	73	31.6				158	68.4
Second trimester	62	10	16.1				52	83.9
Third trimester	13	0	0				13	100.0
Unknown	72	5	6.9				67	93.1
Total	378	88	23.3				290	76.7

*Low n or unknown categories in grey were not included in the chi-square comparisons. †Indicates significant chi-square test of independence (p<0.05) when comparing percentages of mothers who received 17P and those who did not. ‡Indicates significant chi-square test of independence (p<0.01).

Table 1, out of these 378 eligible women, 88 (23.3%) received 17P.

In our study group, greater utilization of 17P was noted in women who received prenatal care (n=88, 25.2%) when compared to women with no prenatal care (n=19, 0%, p<0.05). The intervention was received more frequently by women who initiated prenatal care (PNC) in the first trimester (31.6%) than for women who initiated PNC in the second (16.1%) or third trimester when they missed the GA window of receiving 17P (p<0.01).

Association of 17P treatment was higher in the group of women who had an interpregnancy interval of 18 months or more (29.4%) compared to women who had an interpregnancy interval of less than 18 months (17.7%, p<0.05). In addition, the utilization of 17P was greater in the women with private insurance (44.4%)

Table 2. Adjusted odds ratios for the association between selected maternal characteristics with the receipt of 17P (n=358).

Maternal characteristics	aOR	95 % CI lower	95% CI upper	p-value
Maternal age 35+	1.169	0.518	2.64	0.707
BMI 35+	1.152	0.591	2.244	0.678
Short IPI <18 months	0.682	0.394	1.18	0.171
Maternal race/Ethnicity				
Asian	0.56	0.216	1.451	0.233
Black or African American	0.356	0.111	1.14	0.082
Hispanic or Latina	0.661	0.317	1.376	0.268
White	REF			
Insurance payer status				
Public	REF			
Private*	2.739	1.281	5.855	0.009

*Indicates significance at p<0.01. **aOR:** adjusted odds ratio; **REF:** reference category.

compared to those who had public insurance (19.9%, p<0.001).

Multivariate logistic regression analysis was performed for maternal age, BMI, inter-pregnancy interval (IPI), ethnicity, and insurance status (**Table 2**). Our results show that those with private insurance are more than twice as likely to receive 17P than those with public insurance, (aOR=2.74, 95% CI: 1.98–6.51, p=0.009).

A summary of various treatments received by mothers with a history of SPTD is shown in **Table 3**. Out of the total 378 mothers who had a history of SPTD, 121 (32.0%) received one or more of the three interventions (17P, vaginal progesterone, or cerclage). Among these, 78 (20.6%) of mothers with a history of SPTD received 17P alone and 88 (23.3%) either received 17P alone, 17P and cerclage, or 17P and vaginal progesterone. Only a very small percentage of (2.7%) received 17P with other interventions. The total number of mothers who did not receive any intervention or treatment was 257 (68.0%).

Among the 378 women who were eligible for 17P, 290 women (76.7%) did not receive 17P (**Table 1**). **Fig. 1** shows the frequency of the multiple reasons the eligible women did not receive 17P, as documented in the electronic medical records (n=290). The most commonly reported reasons they did not receive the intervention included missing the eligible time frame (14.8%), treatment declined by patients (6.2%), or denial of insurance approval (2.8%). However, 73.5% had no documented reason or an unknown reason for not receiving the intervention in their medical records.

The process and barriers of receiving 17P, as informed by the provider survey and chart review are mapped out in **Fig. 2**. The provider survey included multiple types of healthcare providers; physicians made up 32% (n=13) of the sample population of providers that were surveyed, and the remainder were other clinical staff and office managers. Provider survey responses (**Fig. 2**) for not prescribing 17P for eligible women included lack of knowledge about the intervention (17%), patient's late entry to care (15%), lack of adequate evidence about the effectiveness of 17P in preterm birth prevention (5%), and patients non-compliance to treatment (5%).

Discussion

Our study results showed that out of the total 378 women who were eligible for 17P, 76.7% (n=290) did not receive 17P intervention. In order to obtain the full

Table 3. Intervention summary for mothers with a previous spontaneous PTD.

Intervention type	n	%
17P only	78	20.6
Vaginal progesterone only	14	3.7
Cerclage only	15	4.0
17P and cerclage	7	1.9
17P and vaginal progesterone	3	0.8
Cerclage and vaginal progesterone	4	1.1
None	257	68.0
Total	**378**	

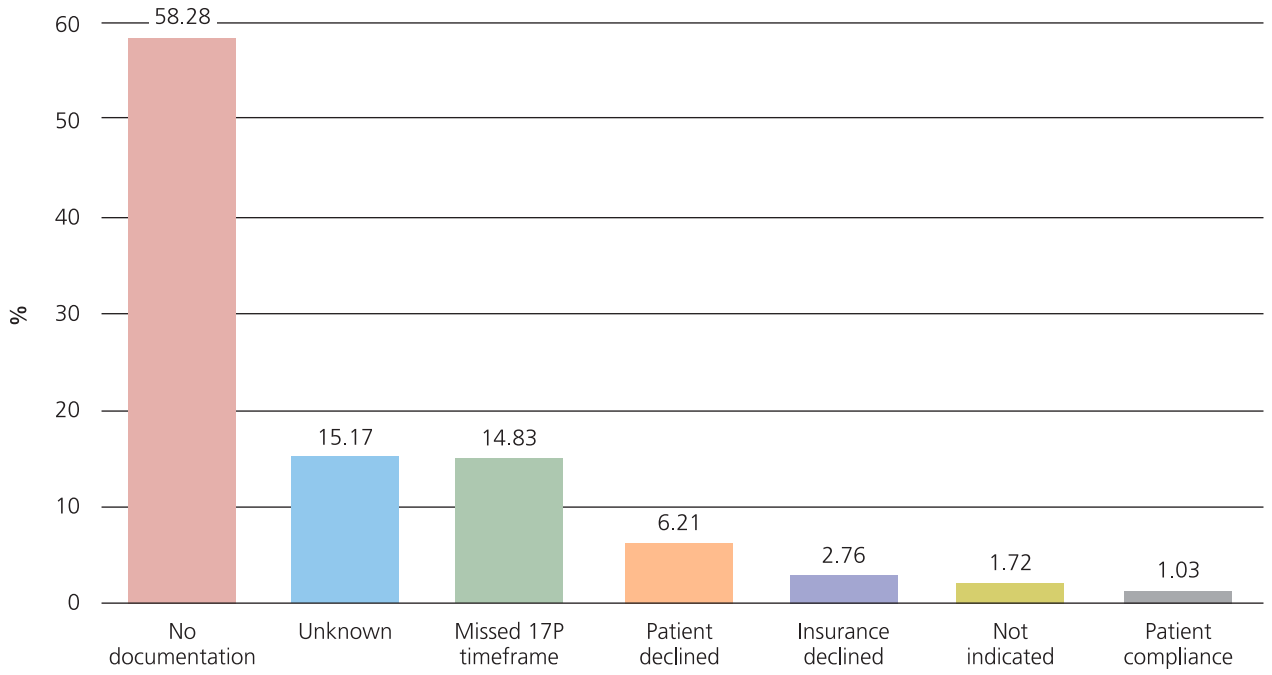

Fig. 1. Reasons eligible patients (history of spontaneous preterm delivery) did not receive 17P.

benefit of 17P, eligible women have to navigate a path that has many roadblocks related to provider, patient and system barriers. The first step in the process that is a major limiting factor is the identification of at-risk mothers followed by the gestational age for onset of prenatal care. Pregnant mothers who presented late to prenatal care missed the window of opportunity for interventions to be implemented. Late prenatal care identified here as a major limiting factor has been reported by Cross-Barnet et al., as a significant reason for under-utilization of 17P in the Medicaid patient population.[24] Although many studies have looked at the efficacy of 17P in preterm birth prevention, very few studies have looked at understanding the potential barriers to the utilization of 17P. Effective utilization of 17P depends on factors at various levels of care that involves patients, providers and the healthcare system.

Barriers to utilization

Among the eligible women, 73.5% with no had no documented reason or an unknown reason for not receiving the intervention in their medical records may indicate incomplete documentation by providers or lack of detailed discussion addressing the beneficial use of 17P. It may also indicate problems with discrepancies in the documentation in the electronic medical records system in use at the medical institution of study.

During the initial prenatal encounter visit, not all patients may have been screened for preterm birth risk; however, we only identified a small percentage of doctors who said identifying patients was a barrier (5%). This small percentage reflects the various provider's practice care models in the community as once patients are identified as high risk for preterm birth, the patients are in majority of cases co-managed with a specialist or referred out for prenatal care with a high risk specialist for the remainder of their pregnancy. This alone becomes a possible barrier for the intervention, as provider shortages may delay the time when the patient is first able to see the specialist provider to discuss possible interventions. Of those surveyed, 15% of providers identified late entry to care as a barrier which was an interesting observation as it mirrored the chart review findings that identified 15% of the patients did not receive the intervention due to late initiation of prenatal care.

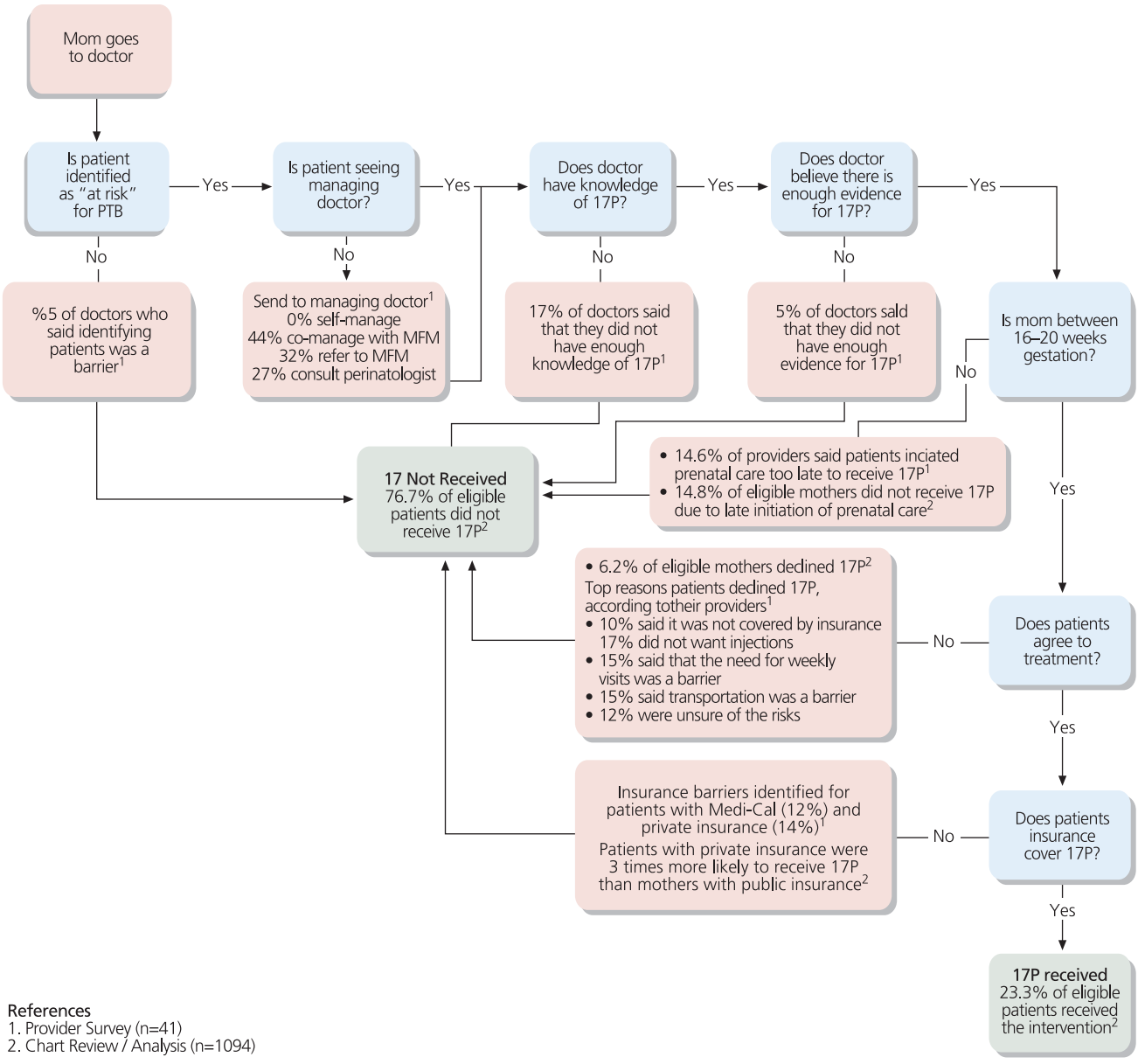

Fig. 2. Health seeking barriers to receiving 17-OHPC.

The most frequently identified barrier in both the provider survey and chart reviews was the lack of insurance coverage for the intervention. This was both a perceived barrier by patients opting out of the treatment when offered, and an actual barrier for patients with public insurance. The perception by providers was that there were more barriers for mothers with private insurance, given that some private insurance may not always cover the treatment costs. However, in the end, those with private insurance seem to be able to overcome barriers more than their publicly insured counterparts.

There was also a disparity for mothers with public insurance, even though 17P intervention is covered. There was a perception of the patients that she would

not be eligible. Our study results showed that, privately insured patients were more likely to end up receiving the intervention. These insurance barriers identified in our study based on the feedback from our provider group survey results is in contrast to provider barriers reported by Danilack et al., who reported a higher percentage of patients with public insurance received 17P intervention compared to those with private insurance.[18]

There were system level barriers that included lack of insurance coverage, insurance restrictions and non-user friendly processes for obtaining prior authorization for the eligible patients. These barriers negatively influenced provider's level of care in optimizing the implementation of the 17P intervention. Thus, the majority of providers seemed to have referred these patients out to specialist care and sometimes this may have caused undue delays in the initiation of the intervention.

Chart reviews and patient interviews gave insight into some of the other reasons for patient barriers for the underutilization of 17P. The reasons patients did not receive 17P as per EMR documentation included patients declining (6.2%), missing the eligible GA time frame (14.9%), insurance declining (2.8%), some did not meet eligibility criteria (1.7%) and patient non-compliance (1.1%). There were 73.5% of eligible patients who had no documented reason for not receiving the intervention in electronic medical records once again pointing to the EMR documentation deficiency.

One of the reasons for patients' tendency to decline the intervention appeared to be influenced by previous pregnancy history. Mothers who had a prior preterm birth near term with shortened length of stay of the neonate in the neonatal intensive care unit or those whose newborns were not admitted to the neonatal intensive care unit were more likely to decline the 17P. This most likely was secondary to a patient's lack of knowledge and awareness that a prior preterm birth not only increases her risk of recurrent preterm birth but that it can occur at a more preterm gestation increasing neonatal morbidity and mortality. Thus, there appeared to be a general lack of perception of the significance of 17P not only in prevention of recurrent preterm birth but also in the reduction of adverse perinatal or neonatal outcomes. These patient barriers that stem from a lack of knowledge and awareness of the adverse long-term sequelae of prematurity is comparable to the results published by Kalata et al., in 2019 that identified patient's lack of knowledge and awareness as the leading cause for the barriers to the intervention indicating sub-optimal counselling by providers regarding the importance of available interventions for prevention of preterm birth.[25]

Provider and patient surveys' feedback and electronic medical records documentation also revealed other reasons such as the hassle of weekly injections, cost to the patients and the issues related to transportation and childcare with the weekly clinic visits. These patient barriers identified in our study contrasts with Kalata et al., who reported the time commitment, specifically the length of clinic appointments and concerns about the safety of the 17P injection as main reasons for patients declining the intervention.[25]

Conclusion

Our study confirmed that 17P intervention for recurrent preterm birth prevention is significantly underutilized in Fresno County, CA, and disproportionately affects patients who have public insurance in addition to a high percentage of patients with inadequate or late prenatal care. The barriers to utilization of 17P were identified at provider, patient and system levels. One approach to overcome some of these barriers to 17P utilization would be to increase provider and patient knowledge and awareness of the adverse neonatal outcomes with preterm birth and educate them on the available resources for care and intervention for prevention of preterm birth. One of the solutions to address the system level barriers would be to streamline the insurance authorization process and obtain a buy in from insurance companies for initiating home nurse visits for obstetrical care for the high-risk patients who may have difficulty with making timely clinic visits for care and interventions.[18,24] An organized and systematic approach to addressing these barriers with education to increase knowledge and awareness of long-term adverse sequelae of preterm birth across the community and system can help reduce preterm birth rate.

Implications for Practice and/or Policy

Preterm birth has a significant negative impact on the public health sector. Preterm birth occurs disproportionately in the lower socioeconomic population group resulting in a significant medical expense burden for the public assisted health insurance system.

The costs extend far beyond the immediate medical costs as these preterm babies can have long term adverse health issues. Development and implementation of public health policies and strategies at the community level of care can improve outcomes and reduce societal costs. The early recognition and detection of those at risk for preterm birth with initiation of interventions for prevention can help reduce adverse pregnancy outcomes for the high-risk patient populations.

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