Time to Completion of Two-Step Screening for Gestational Diabetes and Adverse Outcomes

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Abstract

Objective This study aimed to ascertain whether the length of time to complete the gestational diabetes mellitus (GDM) screening was associated with adverse neonatal outcomes.

Study Design This was a retrospective cohort study of singleton, nonanomalous individuals who were screened for GDM at ≥24 weeks' gestation at an academic hospital system. We compared outcomes among people who were diagnosed with GDM and completed the 3-hour glucose tolerance test (GTT) ≤14 second versus >14 days from the 1-hour glucose challenge test (GCT). The primary outcome was a composite adverse neonatal outcome of the following: large for gestational age, shoulder dystocia, birth injury, respiratory distress, hypoglycemia, or fetal/neonatal death. The secondary outcomes included several individual neonatal and maternal morbidities. Multivariable Poisson's regression models were used to evaluate the association. Adjusted relative risk (aRR) and 95% confidence intervals (CI) were calculated.

Results Among the 313 individuals who completed the two-step screening for GDM and had an 1-hour GCT ≥ 135 mg/dL; of them, 171 (54.6%) completed the 3-hour GTT ≤14 days, 142 (45.4%) completed the 3-hour GTT > 14 days. Overall rate of the primary outcome was 44.1%. After multivariable adjustment, the risk of the primary outcome was similar between people who completed the two-step method in ≤14 versus >14 days (aRR = 1.11, 95% CI = 0.81–1.52). There was no significant difference in all secondary adverse outcomes between the two groups. Subgroup analyses, limited to people diagnosed with GDM ($N = 89$, 23.4%), also found similar results as the full analyses.

Conclusion Among individuals who completed the two-step screening for GDM, completion of the 3-hour GTT within ≤14 versus ≥ 14 days was not associated with an increase rate of the adverse outcomes.

Keywords
- gestational diabetes
- screening
- glucose tolerance test
- large for gestational age

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Key Points

- Among pregnant people in an academic practice, 50% of people with abnormal 1-hour GTT completed GDM two-step screening in 14 days.
- Longer length of time to completion of diagnostic testing for GDM was not associated with an increased rate of adverse outcomes.
- Pregnant people that were diagnosed with GDM and completed the two-step method in >14 days did not have worse perinatal outcomes.

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance during pregnancy, affects up to 10% of all pregnancies in the United States.[1] GDM is associated with maternal and fetal complications such as hypertensive disorders, cesarean section, large for gestational age, shoulder dystocia, neonatal hypoglycemia, and neonatal intensive care unit (NICU admissions).[2–6] Moreover, pregnant people diagnosed with GDM are at up to 60% risk of developing type 2 diabetes later in life.[7–9] Timely diagnosis and treatment of GDM improves short-term maternal and fetal outcomes.[2,3,10,11]

To diagnose GDM, American College of Obstetrics and Gynecologists (ACOG) recommends the two-step method, which entails completion of the screening 1-hour glucose challenge test (GCT); if elevated (≥135–140 mg/dL), the completion of the 3-hour glucose tolerance test (GTT) is required for diagnosis.[12–14] Approximately, 90% of maternal–fetal medicine specialists recommend diagnosis with the two-step method.[15] Unfortunately, the diagnostic 3-hour GTT requires a fasting state and a lengthy clinic visit, which may lead to a delay in testing, diagnosis, and ultimately intervention for GDM.[16]

There are no current guidelines on the optimal length of time to completion of the two-step method for GDM screening. In addition, there is a lack of data in examining the relationship between length of time to completion of the GDM, two-step screening method, and adverse outcomes. The aim of our study was to determine if the length of time to completion of the two-step method GDM screening was associated with adverse neonatal and maternal outcomes.

Materials and Methods

This was a retrospective cohort study taken place at the UT Health (University of Texas Health Science Center at Houston) McGovern Medical School, an academic, tertiary care system in Houston, TX from May 2021 to May 2022. An electronic medical record chart review was conducted to identify all singleton, nonanomalous pregnant people who were screened for GDM at ≥24 weeks' gestation. Exclusion criteria included: people with pregestational diabetes, normal 50-g 1-hour GCT (<135 mg/dL) or individuals that did not complete 3-hour GTT. Pregnant people with 1-hour GCT ≥ 135 mg/dL were considered positive screening based on an institutional threshold. After completion of the diagnostic 100-g 3-hour GTT, diagnosis of GDM was based on Carpenter–Coustan criteria of ≥ 2 abnormal values (fasting blood glucose >90 mg/dL, 1 hour > 180 mg/dL, 2 hour > 155 mg/dL, 3 hour > 140 mg/dL) [7]. We compared outcomes among those who completed the 3-hour GTT in ≤14 versus >14 days from the 1-hour GCT, irrespective of whether they had GDM.

The study was approved by the Institutional Review Board at UTHealth McGovern Medical School (IRB no.: HSC-MS-22-0292). Data were collected from the clinic and hospital medical record system. Maternal records were culled for prenatal visits, including laboratory values, diagnosis of GDM, need for hypoglycemic agents, and ultrasounds. Hospital records were abstracted for admissions during pregnancy, labor, delivery, and postpartum events. Neonatal records were also accessed for birth weight, Apgar scores, length of hospital stay, need for NICU admission, or any other neonatal complications after delivery.

The explanatory variable in this study was time to completion of the 3-hour GTT from the 1-hour GCT, categorized as ≤14 versus > 14 days. As there is no recommended time to completion of two-step GDM screening, the authors arbitrarily designated 14 days to completion as the cutoff between the two groups. The hypothesis was that 14 days is a clinically practical amount of time to allow for completion of screening as well as initiation of GDM care, if required, and greater than 14 days may impact perinatal outcomes.

The primary outcome was a composite neonatal morbidity and mortality (CNM) consisting of any of the following: large for gestational age (defined as birth weight > 90% for gestational age per Duryea et al nomogram),[17] shoulder dystocia or birth injury, respiratory distress, neonatal hypoglycemia, or fetal or neonatal death. Shoulder dystocia or birth injury was defined as additional maneuvers other than gentle downward traction for delivery. Birth injury included clavicular fracture or brachial plexus injury. Respiratory distress was defined as the need for at least 4 hours of respiratory support with supplemental oxygen, continuous positive airway pressure, or ventilation at the first 24 hours of life. Neonatal hypoglycemia was defined as blood glucose < 40 mg/dL in the first 24 hours of life or <50 mg/dL after or requiring medical therapy.

The secondary adverse neonatal outcomes included: rates of preterm delivery, Apgar score <7 at 5 minutes, need for continuous positive airway pressure ventilation neonatal jaundice requiring phototherapy, and length of hospital stay. Secondary adverse maternal outcomes that were collected included: hypertensive disorders of pregnancy, chorioamnionitis, cesarean delivery (CD), postpartum hemorrhage, endometritis, or postpartum readmission ≤6 weeks. Preterm birth was defined as delivery at <37 weeks' gestation. Hypertensive disorder of pregnancy included gestational hypertension, preeclampsia, or superimposed preeclampsia based on the

current Task Force Criteria for Hypertension in pregnancy.[18] Gestational hypertension defined as new onset hypertension (systolic ≥ 140 mm Hg or diastolic ≥ 90 mm Hg) without proteinuria (either ≥300 mg per 24 hours or protein/Cr ratio ≥ 0.3) after 20 weeks of gestation. Preeclampsia defined as hypertension (systolic ≥ 140 mm Hg or diastolic ≥ 90 mm Hg) with proteinuria or serum laboratory abnormalities (platelets ≤ 100,000, serum aspartate aminotransferase ≥ 80 IU/mL, creatinine ≥ 1.1 mg/dL). Preeclampsia with severe features defined as systolic ≥ 160 mm Hg, diastolic ≥ 110 mm Hg, persistent headache, pulmonary edema, or any serum laboratory abnormalities as above.

Statistical Analysis

We examined the differences in baseline characteristics and outcomes between time groups (completion of 3-hour GTT in ≤14 versus > 14 days from abnormal 1-hour GCT) using the chi-square test or Fischer's exact test for categorical variables and Student's *t*-tests for continuous variables. Multivariable Poisson regression models were used to evaluate the association between time groups (≤ 14 days [reference] vs. >14 days) and the primary outcome, while adjusting for maternal age (<20, 20–34, ≥35 years), maternal race, and ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic-Other, unknown), private insurance (private, government-issued insurance or no insurance), nulliparity, obesity (body mass index [BMI] ≥ 30 kg/m^2), hypertensive disorder, thyroid disease and gestational age at time of 1-hour GCT. The results were presented as adjusted relative risk (aRR) with 95% confidence interval (CI). Using the same approach, we also performed subgroup analyses among those diagnosed with GDM. Statistical significance was noted to be a *p*-value of < 0.05 or if the 95% CI did not include the integer 1. Statistical analysis was completed using STATA software, version 17 (Stata-Corp., College Station, TX).

Results

Among the 401 pregnancies with 1-hour GCT ≥ 135 mg/dL during the study period, 342 (85.3%) pregnant people had 3-hour GTT ordered. A total of 59 individuals did not have 3-hour GTT ordered due to the following reasons: GDM was diagnosed based on elevated 1-hour GCT ($N = 25$) and 3-hour GTT not ordered by primary obstetrician ($N = 34$). A total of 29 people did not complete the ordered 3-hour GTT.

The final study sample included 313 (78.1%) pregnant people who completed the 3-hour GTT. Among our study population, 171 (54.6%) completed the two-step method in ≤ 14 days and 142 (45.4%) completed >14 days (►**Fig. 1**).

Baseline characteristics for the two groups were similar except for insurance status (►**Table 1**). Those who completed the 3-hour GTT >14 days were more likely to be insured with Medicaid (≤14 days 45% vs. >14 days 74%, $p = 0.004$).

Overall, the rate of the primary outcome was 28.8%; 25.7% in the group of ≤14 days, whereas 32.4% in the group of >14 days ($p = 0.195$). The most common component of the primary outcome was neonatal hypoglycemia (15.7%; 14.0% in ≤14 days and 17.6% >14 days, $p = 0.387$). After multivariable adjustment, the risk of the primary outcome was similar between people who completed the two-step method in ≤14 days versus >14 days (aRR = 1.11; 95% CI = 0.81–1.52,). There was no difference in any component of the primary outcome between the two groups (►**Table 2**).

►**Table 3** presents the secondary adverse neonatal and maternal outcomes. The results showed that there was no

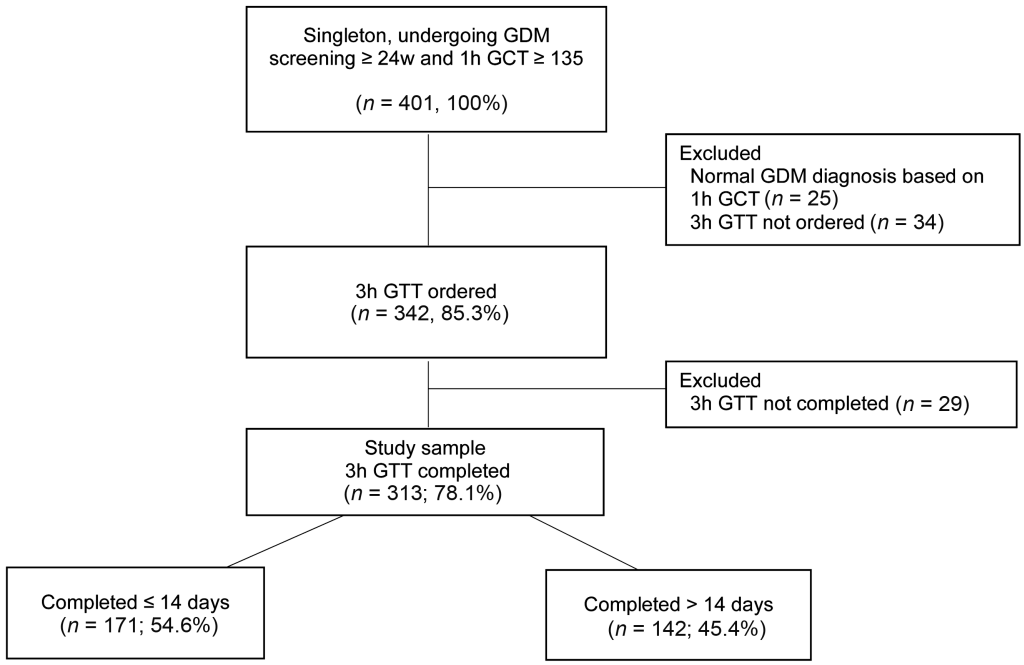

Fig. 1 Flow chart of pregnant people: eligibility and sample size. GDM, gestational diabetes; 1hGCT, 1-hour glucose challenge test; 3hGCT, 3-hour glucose tolerance test.

Table 1 Baseline characteristics

Characteristics	Two-step completed		*p*-Value
	≤14 d	>14 d	
	n = 171 (%)	*n* = 142 (%)	
Maternal age (y)			
< 20	5 (2.9)	6 (4.2)	0.550
20–34	134 (78)	104 (73)	
≥35	32 (18.7)	32 (22.5)	
Race/ethnicity			
Non-Hispanic White	47 (27)	28 (20)	0.100
Non-Hispanic Black	20 (12)	29 (20)	
Hispanic	27 (16)	21 (15)	
Other	69 (40)	52 (37)	
Unknown	8 (4.7)	12 (8.5)	
Insurance status			
Private	94 (55.0)	62 (44)	0.004
Medicaid	77 (45.0)	74 (52.1)	
Self-pay/no insurance	0 (0.0)	6 (4.2)	
Nulliparous	27 (15.8)	27 (19.0)	0.452
Obese (BMI ≥ 30 kg/m^2)	85 (49.7)	67 (47.2)	0.656
Hypertension	13 (7.6)	12 (8.5)	0.783
Thyroid disease	12 (7.0)	8 (5.6)	0.618
Substance use (tobacco or illicit drug)			
Yes	5 (2.9)	5 (3.5)	0.496
No	150 (87.7)	118 (83.1)	
Unknown	16 (9.4)	19 (13.4)	
GA at screening 1 h GCT	26.4 (2.0)	26.7 (2.1)	0.321
1 h GCT	157.0 (16.7)	155.4 (15.8)	0.395
1 abnormal value of 3 h GTT[a]	73.0 (42.7)	50.0 (35.2)	0.177
Diagnosis of GDM	48.0 (28.1)	41.0 (28.9)	0.875
Diabetes educator visit	42.0 (24.6)	36.0 (25.4)	0.872
Need for hypoglycemic agent	23.0 (13.5)	11.0 (7.7)	0.106

Abbreviations: BMI, body mass index; CGM, continuous glucose monitoring; GA, gestational age; GCT, glucose challenge test; GTT, glucose tolerance test.
Note: Data are presented as number (percentage) or mean (standard deviation).
[a]GTT defined as abnormal based on Carpenter–Coustan criteria of ≥ 2 abnormal values: fasting blood glucose > 90, 1 hour > 180, 2 hours > 155, 3 hours > 140 mg/dL.

difference in all the secondary adverse outcomes between the time groups. The most common maternal complication was CD (40.4% in ≤14 days and 43.7% in >14 days, $p = 0.554$; ►Table 3).

There were a total of 89 (28.4%) pregnant people that were diagnosed with GDM. Of them, 48 (53.9%) people completed the two-step method in ≤14 days and 41 (46.1%) people completed in >14 days. Subgroup analysis showed there was no significant difference in any component of the CNM between the two groups, similar to the primary analysis (aRR = 1.01; 95% CI = 0.59–1.78). The most common CNM in both groups was neonatal hypoglycemia (29.2% in ≤14 days and 29.3% >14 days). In addition, we did not find any differences in all secondary neonatal and maternal outcomes in those diagnosed with GDM (►Table 4).

Discussion

In this retrospective cohort study of the length of time to completion of two-step method for diagnosis of GDM, there was no association with worse adverse neonatal or maternal outcomes in people with longer period of time to completion of testing. In our study, we observed that approximately 50% of people that received care at our institution completed the two tests within 14 days, while 67% of people completed the two-step method in ≤21 days.

Table 2 The primary outcome: composite neonatal adverse outcome

	Two-step method		*p*-Value	Adjusted RR (95% CI)
	Completed in ≤14 d *n* = 171 (%)	Completed in > 14 d *n* = 142 (%)		
Composite neonatal outcome	44 (25.7)	46 (32.4)	0.20	1.21 (0.85–1.73)
Large for gestational age[a]	14 (8.2)	14 (9.9)	0.61	
Shoulder dystocia or birth injury[b]	5 (2.9)	5 (3.5)	0.77	
Respiratory distress[c]	8 (4.7)	14 (9.9)	0.07	
Hypoglycemia[d]	24 (14.0)	25 (17.6)	0.39	
Fetal or neonatal death	0 (0)	0 (0)	N/C	

Abbreviations: CI, confidence interval; CPAP, continuous positive airway pressure; N/C, not calculable; RR, relative risk.
Notes: Data are presented as number (percentage) or median (standard deviation). Adjusted for insurance status.
[a]Birth weight above 90th percentile using the nomogram by Duryea et al.
[b]Need for any extra maneuvers for delivery, clavicular fracture, or brachial plexus injury.
[c]Need of at least 4 hours of respiratory support with supplemental oxygen, continuous positive airway pressure, or ventilation at the first 24 hours of life.
[d]Blood glucose <40 mg/dL in the first 24 hours of life or <50 mg/dL after or requiring medical therapy.

Table 3 The secondary neonatal and maternal adverse outcome

Outcomes	Two-step method		*p*-Value
	Completed in ≤14 d *n* = 171 (%)	Completed in > 14 d *n* = 142 (%)	
Neonatal adverse outcomes			
Preterm delivery (<37 wk)	23 (13.5)	26 (18.3)	0.239
Birth weight (g)	3,214.4 (± 467.0)	3,149.1 (±566.6)	0.265
Apgar score <7 at 5 min	1 (0.6)	0 (0.0)	1.000
CPAP	11 (6.4)	11 (7.7)	0.651
Neonatal jaundice requiring phototherapy	25 (14.6)	16 (11.3)	0.381
Length of hospital stay (d)	2.6 (± 2.8)	3.4 (± 6.2)	0.118
Maternal adverse outcomes			
Hypertensive disorders of pregnancy[a]	39 (24.9)	37 (28.2)	0.474
Preeclampsia with severe features	11 (6.9)	6 (4.6)	0.444
Chorioamnionitis	6 (3.5)	10 (7.0)	0.158
Cesarean delivery	69 (40.4)	62 (43.7)	0.554
Postpartum hemorrhage	9 (5.3)	7 (4.9)	0.894
Endometritis	2 (1.2)	1(0.7)	1.000
Postpartum readmission ≤6 wk	7 (4.3)	4 (2.9)	0.557

Abbreviation: CPAP, continuous positive airway pressure.
Note: Data are presented as number (percentage) or mean (standard deviation).
[a]Hypertensive disorder of pregnancy including gestational hypertension, preeclampsia, or superimposed preeclampsia.

In addition, subgroup analyses of those that were diagnosed with GDM did not show a significantly higher rate of adverse outcomes among those that took >14 days to diagnosis. Majority of people were able to be diagnosed with GDM in less than a month's time allowing for appropriate intervention.

There have been no prior studies examining length of time to completion of GDM screening and neonatal and maternal morbidity. However, many studies have explored the barriers to completion of the 1-hour GCT. Several social and institutional factors have been identified: inability to tolerate test, compliance with multiple prenatal appointments, younger maternal age, and mental/social stressors.[19,20] These prior reports are consistent with our findings of those who completed the GDM screening in ≤14 days had a significantly higher rate of private insurance as compared with >14 days to completion ($p = 0.004$). Although we did not find a significant difference in the primary outcome based on the length of time to completion of the two-step method of GDM screening, we detected a higher-than-average rate of neonatal hypoglycemia. Prior research reported that up to 10% of low risk, term newborns experience

Table 4 Subgroup analyses: the primary and secondary outcomes in those diagnosed with gestational diabetes mellitus

	Two-step method		*p*-Value	Adjusted RR (95% CI)
	Completed in ≤14 d *n* = 48 (%)	Completed in >14 d *n* = 41 (%)		
Composite neonatal outcome	18 (37.5)	17 (41.5)	0.703	1.01 (0.59–1.78)
Large for gestational age[a]	4 (8.3)	4 (9.8)	1.000	
Shoulder dystocia or birth injury[b]	1 (2.1)	2 (4.9)	0.593	
Respiratory distress[c]	1 (2.1)	4 (9.8)	0.176	
Hypoglycemia[d]	14 (29.2)	12 (29.3)	0.992	
Fetal or neonatal death	0 (0.0)	0 (0.0)	N/C	
Secondary neonatal outcomes	5 (10.4)	10 (24.4)	0.17	
Preterm delivery (<37 wk)	5 (10.4)	10 (24.4)	0.079	
Birth weight (g)	3,221.7 (±452.3)	3,114.3 (±612.7)	0.345	
Apgar score <7 at 5 min	1 (2.1)	0 (0.0)	1.000	
CPAP	3 (6.3)	4 (9.8)	0.699	
Neonatal jaundice requiring phototherapy	2 (4.2)	5 (12.2)	0.241	
Length of hospital stay (d)	2.3 (± 1.5)	3.9 (± 5.9)	0.079	
Secondary maternal outcomes				
Hypertensive disorders of pregnancy[e]	7 (14.9)	12 (29.3)	0.102	
Chorioamnionitis	1 (2.1)	5 (12.2)	0.091	
Cesarean delivery	22 (45.8)	25 (61.0)	0.154	
Postpartum hemorrhage	3 (6.3)	3 (7.3)	1.000	
Endometritis	0 (0.0)	0 (0.0)	N/C	
Postpartum readmission ≤ 6 wk	4 (8.7)	2 (5.3)	0.685	

Abbreviations: CI, CPAP, continuous positive airway pressure; N/C, not calculable; RR, relative risk.
Notes: Data are presented as number (percentage) or median (standard deviation). Adjusted for insurance status.
[a]Birth weight above 90th percentile using the nomogram by Duryea et al.
[b]Need for any extra maneuvers for delivery, clavicular fracture or brachial plexus injury.
[c]Need of at least 4 hours of respiratory support with supplemental oxygen, continuous positive airway pressure, or ventilation at the first 24 hours of life.
[d]Blood glucose <40 mg/dL in the first 24 hours of life or <50 mg/dL after or requiring medical therapy.
[e]Hypertensive disorder of pregnancy including gestational hypertension, preeclampsia, or superimposed preeclampsia.

hypoglycemia defined as <40 to 45 mg/dL.[21,22] In our study, however, the rate of the neonatal hypoglycemia was 15.7%. The increased rate may be due to high-risk pregnancies (those with GDM diagnosis or 48.5% of patients with BMI ≥30) being included in our study population. This also reflects that hyperglycemia, below the threshold of diagnosis, is associated with worse perinatal outcomes consistent with the Landon et al findings study.[2] Despite completing and passing the two-step screening method, poor neonatal outcomes that are associated with GDM were observed. Future studies should focus on exploring other risk factors for neonatal hypoglycemia and whether the current method for GDM diagnosis in pregnancy is sufficient for diagnosis and treatment of people with elevated blood sugars during pregnancy.

Limitations and Strengths

We acknowledge the limitations of this study. It was a single-center, retrospective analyses and was specific to a university practice. Causes of delay might be due to several and all factors of social determinants of health, reflecting both a clinic system's issue as well as disparities in access to health care.[19,20] We performed a multivariable adjustment analysis on the primary outcome of the composite neonatal adverse outcome. However, this analysis was not completed on the secondary outcomes due to small case numbers, and the bivariate analyses showed that there were no significant results in all the secondary outcomes. Another limitation was the risk of Type 2 error given small cohort sample; a significant difference between the two groups may have been observed with a larger sample size, given the high rate of neonatal hypoglycemia.

Our study has several strengths. To the best of our knowledge, this is the first study that has explored neonatal and maternal outcomes associated with length of time to completion of GDM screening. Although the study population was from a single center, our sample included people from a greater metropolitan area. In addition, our overall rate of GDM detection was approximately 6%, consistent with the overall national average.[5,13,23–25]

Conclusion

In conclusion, we did not find a difference in adverse neonatal and maternal outcomes associated with the length of time to completion of the two-step GDM diagnosing method. This study provides a clinically applicable quantification of the delay that happens almost 50% of the time in the journey to diagnosis of GDM. This highlights that completion of the two-step method is fraught with challenges and a more practical form of GDM screening is needed for the ease of pregnant people.

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Conflict of Interest
None declared.

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