

Management of Maternal Obstetric Complications

Diabetes in Pregnancy- impacting outcomes
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8 November 2024

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Disclosures

- I have no conflicts of interest to disclose.

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Objectives

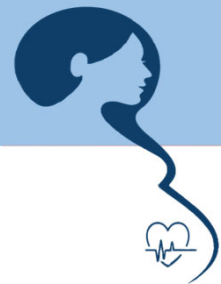


- To discuss physiology of diabetes in pregnancy.
- To explore data surrounding the screening, diagnosis and treatment of GDM in pregnancy.
- To discuss the data regarding treatment of pre-gestational diabetes during pregnancy.
- To discuss risk of diabetes to pregnancy.

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Diabetes during pregnancy

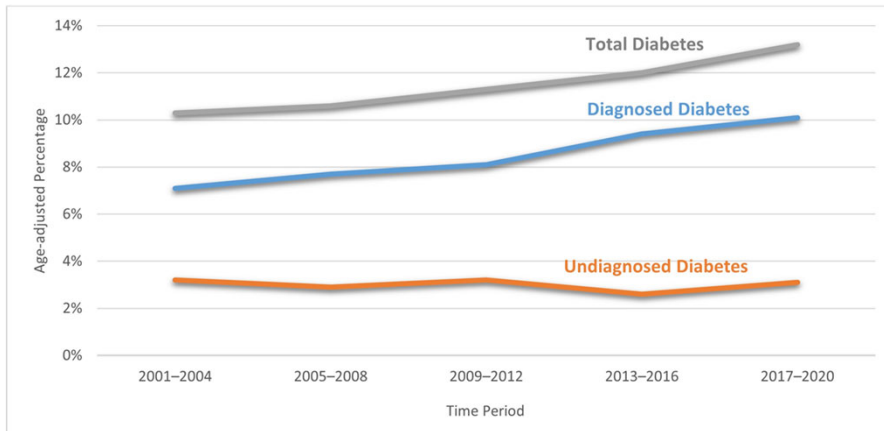


- Diabetes is common
 - 0.2-0.5% type 1
 - 1-2% Type 2
 - 6-9% Gestational
- If using international standard 2-hour testing, Rate of GDM expected to be 2-3x higher (Australia reported 17.9% GDM rate in 2020-2021).
- The US would likely have ~2-3x higher rate of DM in pregnancy

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Rate of diabetes is increasing

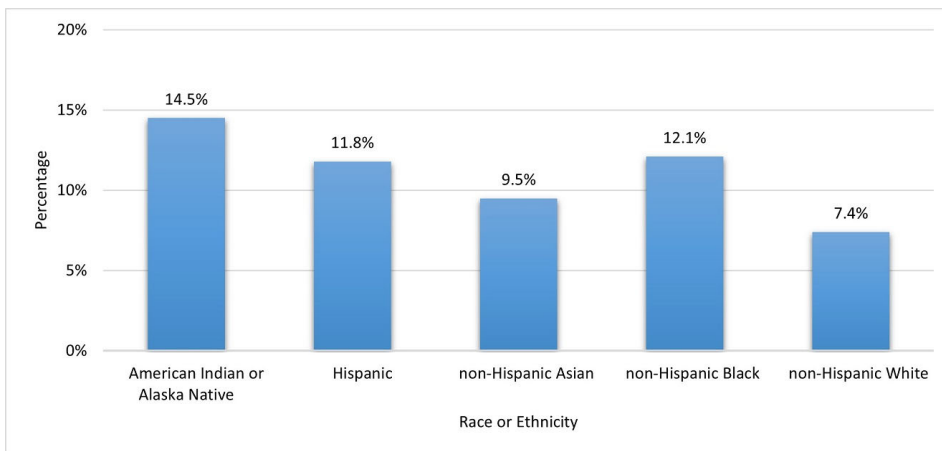
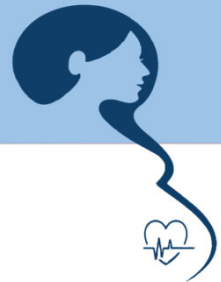


National Health and Nutrition Examination Surveys, Centers for Disease Control and Prevention.



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Diabetes care is a health equity issue



National Health and Nutrition Examination Surveys, Centers for Disease Control and Prevention.



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Why do people get Diabetes?



Type I

Pancreas doesn't make enough insulin

Multiple causes include

Injury to pancreas

Body's immune system attacks and destroys the beta cells that make insulin (autoimmune or viral)

Thought some people are predisposed and environmental factor triggers

Risk factors: family hx (about an 11% risk) and certain genetic conditions

• Type II

- The body still produces insulin, but it's unable to use it effectively.
- Insulin resistance.
- Over time, the demand for insulin overpowers the pancreas' ability to produce it, leading to an insulin deficiency.
- The risk factors for developing T2DM: A family history of diabetes, obesity, a sedentary lifestyle, poor diet, and certain ethnicities
- Aging also increases the risk.



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Why does GDM happen?



- Physiologic changes in pregnancy increase available glucose and mobilize across the placenta.
- Estrogen, progesterone, cortisol and human placenta lactogen (Primary driver of insulin resistance) are hormones that alter how glucose is used in pregnant women and can cause insulin resistance.
- Insulin resistance increases with advancing gestation.

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Why does it matter?



- Maternal blood sugar is major cause of birth defects
 - Rate of birth defects with uncontrolled blood sugar 40%
 - Comparison to Thalidomide (14%)
- Associated with high rate of preeclampsia, thus prematurity
- Increased risk of RDS at all gestational ages
- Increased risk of Shoulder dystocia and birth injury
- Increased risk of CD
- May increase the risk of long-term health problems in offspring (fetal programming)

A1c range (%)	Major fetal malformation	Miscarriage	Perinatal mortality
< 6.9	3.9%		2.1%
6.9-7.8	4.9%	8%	2.8%
7.9-8.8	5.0%	18%	3.3%
10-12	23.5%	20%	6.3%
12.1-15	38.9%	45%	
> 15	40%		

Modified from American Diabetes Association Professional Practice Committee; 15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024. Diabetes Care* 1 January 2024; 47 (Supplement_1): S282–S294. <https://doi.org/10.2337/dc24-S015>

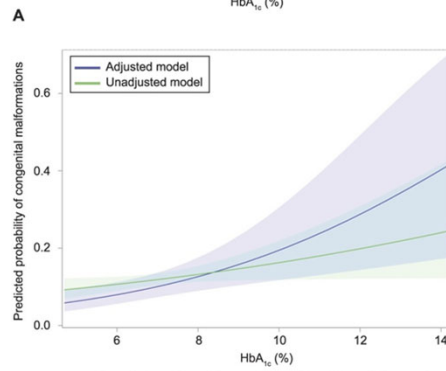
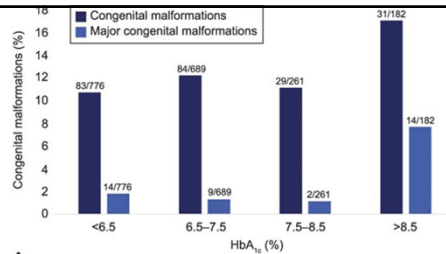


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New Data: Risks are still high

[Glycemic Control and Risk of Congenital Malformations in Women With Type 1 Diabetes](#)

Thorius, Ida Holte; Petersen, Janne; Husemoen, Lise Lotte N.; Alibegovic, Amra C.; Gall, Mari-Anne; Damm, Peter; Mathiesen, Elisabeth R. *Obstetrics & Gynecology*144(5):725-732, November 2024. doi: 10.1097/AOG.0000000000005722




HbA _{1c} (%)	5.5	6.5	7.5	8.5	9.5	10.5	11.5	12.5	13.5
Unadjusted absolute risk (%)	10.1	11.2	12.4	13.9	15.4	17.0	18.8	20.7	22.9
Adjusted absolute risk (%)	6.9	8.8	11.2	13.9	17.3	21.3	25.9	31.2	36.9



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USPSTF GDM Screening recommendations




What does the USPSTF recommend?	<p>Pregnant persons at 24 weeks of gestation or after</p> <ul style="list-style-type: none"> • Screen for gestational diabetes. <p>Grade: B</p> <hr/> <p>Pregnant persons before 24 weeks of gestation</p> <ul style="list-style-type: none"> • The evidence is insufficient to assess the balance of benefits and harms for screening for gestational diabetes. <p>Grade: I statement</p>
To whom does this recommendation apply?	Pregnant persons who have not been previously diagnosed with type 1 or type 2 diabetes.
What's new?	This recommendation is consistent with the 2014 USPSTF recommendation.
How to implement this recommendation?	<p>Screen: If the person is pregnant and is at least 24 weeks of gestation, screen for gestational diabetes by using 1 of several methods:</p> <ul style="list-style-type: none"> • A 2-step process that involves a screening test (oral glucose challenge test) followed by a diagnostic test (oral glucose tolerance test). This is the most common approach in the US. • A 1-step process in which the diagnostic test (oral glucose tolerance test) is administered to all patients. • Fasting plasma glucose measurement.
How often?	One-time screening should be performed at or after 24 weeks of gestation. Typically in the US, screening occurs prior to 28 weeks of gestation; however, it can occur later in persons who enter prenatal care after 28 weeks of gestation.
What are other relevant USPSTF recommendations?	The USPSTF has several recommendations related to pregnancy and the prevention of gestational diabetes. This includes recommendations on screening for abnormal blood glucose levels and type 2 diabetes (B recommendation), behavioral weight loss interventions to prevent obesity-related morbidity and mortality in adults (B recommendation), and behavioral counseling interventions for healthy weight and weight gain during pregnancy (B recommendation). These recommendations are available at https://www.uspreventiveservicestaskforce.org
Where to read the full recommendation statement?	Visit the USPSTF website to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

SCREEN for GDM But How?


US Preventive Services Task Force. Screening for Gestational Diabetes: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021;326(6):531–538. doi:10.1001/jama.2021.11922

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.




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Screening options?



- 24-28 weeks is recommended for all pregnancies
- 2 Step (most common): 50 g 1-hour GCT followed by 100 g 3-hour OGTT?
- Debate about 50 g Cutoffs 130, 135, 140?
- 3 hour Values? NDDG vs Carpenter-Coustan (ACOG recommended)?
- One step 2-hour 75g OGTT?
- HAPO (IADPSG) cutoffs (92, 180, 153)? (95, 180, 155)?
 - Increases diagnosis by 2-3x vs 2 step
 - Does it matter?



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Early screening?



- Routine early screening not currently recommended for all patients.
- Risk factor based early screening?
- 2 Step vs 1 step?
- HgbA1c?
- Fasting glucose?
- Something else?



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1 vs 2 Step

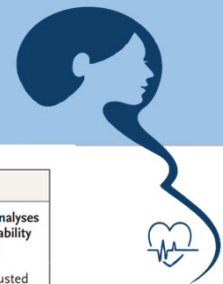


Table 2. Primary Outcomes, According to One-Step or Two-Step Screening for Gestational Diabetes.*

Outcome	Randomized Group		Preplanned Intention-to-Treat Analyses†			Intention-to-Treat Analyses with Inverse Probability Weighting‡
	One-Step Screening (N=11,922)	Two-Step Screening (N=11,870)	Unadjusted Relative Risk (97.5% CI)§	Relative Risk, Adjusted for Gestational Diabetes (97.5% CI)§	Relative Risk, Adjusted for Gestational Diabetes, Prespecified Covariates, and Nonadherence‡§ (97.5% CI)§	Relative Risk, Adjusted for Gestational Diabetes, Prespecified Covariates, and Nonadherence‡§ (97.5% CI)§
	<i>no./total no. (%)</i>					
Gestational diabetes¶	1837/11,127 (16.5)	945/11,162 (8.5)	1.94 (1.79–2.11)	NA	1.93 (1.77–2.11)	1.93 (1.76–2.12)
Large-for-gestational-age infants	977/11,028 (8.9)	1015/10,986 (9.2)	0.95 (0.87–1.05)	0.93 (0.84–1.03)	0.94 (0.85–1.04)	0.92 (0.83–1.02)
Perinatal composite outcome	351/11,281 (3.1)	337/11,213 (3.0)	1.04 (0.88–1.23)	1.08 (0.90–1.30)	1.08 (0.89–1.31)	1.10 (0.91–1.35)
Gestational hypertension or preeclampsia	1490/10,974 (13.6)	1472/10,894 (13.5)	1.00 (0.93–1.08)	0.96 (0.88–1.03)	0.98 (0.90–1.06)	0.98 (0.90–1.06)
Primary cesarean section	2826/11,755 (24.0)	2887/11,714 (24.6)	0.98 (0.93–1.02)	0.95 (0.91–1.00)	0.96 (0.91–1.02)	0.96 (0.91–1.02)

Hillier TA et al. N Engl J Med 2021;384:895-904



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Study conclusions



- Despite more diagnoses of gestational diabetes with the one-step approach than with the two-step approach, there were no significant between-group differences in the risks of the primary outcomes relating to perinatal and maternal complications. *



Adherence to assigned test differed between the two strategies: 66.1% for 1-step and 91.7% for 2-step ($p < .0001$). 27% of the women randomized to receive the 1-step completed the 2-step test vs 2% randomized to the 2-step who completed the 1-step ($p < .0001$).

- Thus, the planned intention-to-treat analysis would likely be biased if alternative statistical methods are not also utilized to account for an imbalance in adherence.
- 165 patients with FBG of >95 on 2 step may have been treated as GDM, but not diagnosed.

Pedula KL, Hillier TA, Ogasawara KK, Vesco KK, Lubarsky S, Oshiro CES, VanMarter J. A randomized pragmatic clinical trial of gestational diabetes screening (ScreenR2GDM): Study design, baseline characteristics, and protocol adherence. *Contemp Clin Trials*. 2019 Oct;85:105829. doi: 10.1016/j.cct.2019.105829. Epub 2019 Aug 16. PMID: 31425751; PMCID: PMC6939663.



TABLE
Primary outcomes, according to 1-step or 2-step screening for gestational diabetes using per-protocol and as-treated analyses^a

Outcome	PP ^b		RR, adjusted for GDM, prespecified covariates, and nonadherence ^d (97.5% CI)	AT ^c		RR, adjusted for GDM, prespecified covariates, and nonadherence ^d (97.5% CI)
	1-step (N = 7880) n/N (%)	2-step (N = 10,881)		1-step (N = 8161) n/N (%)	2-step (N = 14,128)	
GDM	1597/7880 (20.3)	864/10881 (7.9)	2.51 (2.29–2.74)	1678/8161 (20.6)	1104/14128 (7.8)	2.57 (2.36–2.79)
Large for gestational age infants	614/7349 (8.4)	937/10130 (9.2)	0.89 (0.79–0.99)	644/7619 (8.5)	1235/13158 (9.4)	0.89 (0.80–0.99)
Perinatal composite outcome ^e	216/7481 (2.9)	284/10304 (2.8)	1.11 (0.90–1.36)	223/7755 (2.9)	378/13397 (2.8)	1.08 (0.89–1.31)
Gestational hypertension or preeclampsia	1031/7251 (14.2)	1380/9998 (13.8)	0.99 (0.91–1.08)	1069/7502 (14.2)	1754/12980 (13.5)	1.00 (0.92–1.08)
Primary CD	1918/7803 (24.6)	2664/10770 (24.7)	0.97 (0.91–1.03)	1983/8081 (24.5)	3389/13978 (24.2)	— ^f

Data are presented as number/total number (percentage), unless otherwise indicated.
AT, as-treated; CD, cesarean delivery; CI, confidence interval; GDM, gestational diabetes mellitus; PP, per-protocol; RR, relative risk.

^a The denominators vary according to the ascertainment method and exclusion criteria for each outcome. The maternal outcome of gestational hypertension or preeclampsia excluded women with preexisting hypertension before pregnancy. Primary CD excluded women who left the health plan before delivery. The perinatal composite outcome included pregnancies for which information was available in the maternal record (stillbirth and shoulder dystocia) or in newborn records that were matched to maternal records. Reasons for unmatched newborn records include adoption, deliveries within and outside the health plan in which the newborn was covered by other insurance, deliveries outside the health plan for which no reimbursement for newborn care was requested, and instances in which the mother left the health plan before delivery and no information was available for the newborn. ^b PP compares pregnancies randomized to 1-step vs those randomized to 2-step who received 2-step. ^c AT compares pregnancies based on actual test received (1-step or 2-step), regardless of the randomized assignment. If there were >1 GDM diagnostic test performed during pregnancy, then pregnancies were categorized by the last GDM screening test received. ^d Prespecified covariates include race and ethnicity, prepregnancy obesity, and weight gain exceeding the National Academy of Medicine weight gain guidelines. ^e Factors related to nonadherence include maternal age, nulliparity, race and ethnicity, Medicaid insurance, previous GDM, preexisting hypertension, trial site, maternal obesity at first prenatal visit, provider type, and randomized group. The widths of CIs have not been adjusted to account for multiplicity and cannot be used to infer treatment effects. ^f The perinatal composite consisted of any of the following: stillbirth, neonatal death, shoulder dystocia, bone fracture, or any arm or hand nerve palsy related to birth injury. ^g AT analysis for primary CD is stratified by GDM owing to significant interaction term of GDM by the AT group: for pregnancies with GDM (RR, 0.89; 97.5% CI, 0.78–1.02) and for pregnancies without GDM (RR, 0.99; 97.5% CI, 0.94–1.06).

Hillier. Implications from a pragmatic randomized clinical trial of gestational diabetes screening. *Am J Obstet Gynecol*. 2021.

- Hillier TA, Pedula KL, Ogasawara KK, Vesco KK, Oshiro CES, Lubarsky SL, Van Marter J. Further implications from a pragmatic randomized clinical trial of gestational diabetes screening: per-protocol and as-treated estimates. *Am J Obstet Gynecol*. 2021 Nov;225(5):581-583. doi: 10.1016/j.ajog.2021.08.006. Epub 2021 Aug 9. PMID: 34384772; PMCID: PMC9172629.

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Screening for GDM

- With the USPSTF publication of recommendations, this editorial review was published by the NICHD, NIH highlighting the recommendations not to screen before 24 weeks is based on the lack of evidence, and that the current tests may not be the best means of testing in the first trimester.

Zhang C, Catalano P. Screening for Gestational Diabetes. *JAMA*. 2021;326(6):487–489.
doi:10.1001/jama.2021.12190

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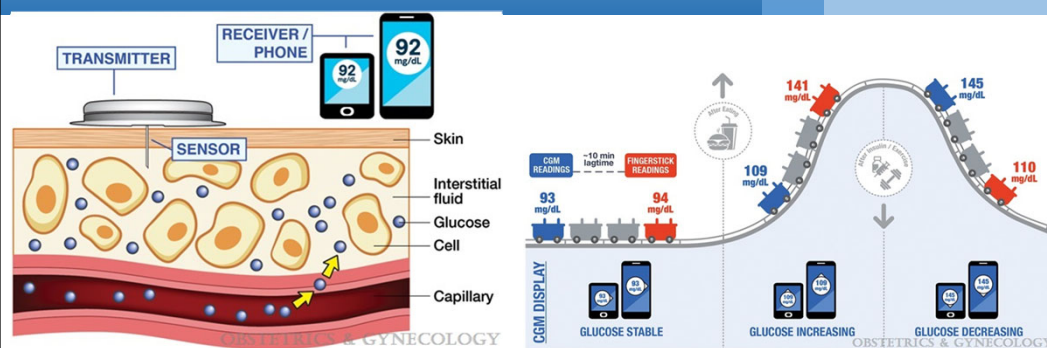
Other future options?

- GO MOMS (CGMS based screening)
 - Ongoing trial to identify glycemic patterns that could predict adverse outcomes and need for early intervention.
 - With OTC CGMS now available, this may become a valid options for screening.
- First trimester non-fasting Plasma lipid profiles may improve detection of GDM
 - Zhu Y, Tsai MY, Sun Q, et al. A prospective and longitudinal study of plasma phospholipid saturated fatty acid profile in relation to cardiometabolic biomarkers and the risk of gestational diabetes. *Am J Clin Nutr.* 2018;107(6): 1017-1026. doi:10.1093/ajcn/nqy051
- Urinary metabolomic marker may accurately predict GDM in the first trimester.
 - Koos BJ, Gornbein JA. Early pregnancy metabolites predict gestational diabetes mellitus: implications for fetal programming. *Am J Obstet Gynecol.* 2021;224(2):215.e1-215.e7. doi:10.1016/j.ajog. 2020.07.050

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CGMS



[Continuous Glucose Monitoring for Diabetes Management During Pregnancy: Evidence, Practical Tips, and Common Pitfalls](#)

Battarbee, Ashley N.; Durnwald, Celeste; Yee, Lynn M.; Valent, Amy M.

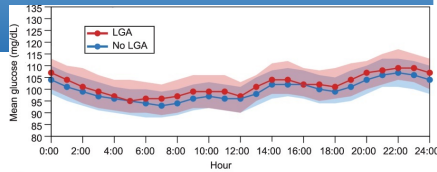
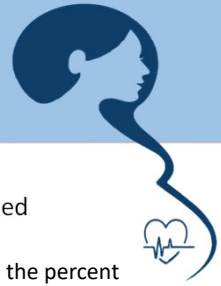
*Obstetrics & Gynecology*144(5):649-659, November 2024.

doi: 10.1097/AOG.0000000000005669

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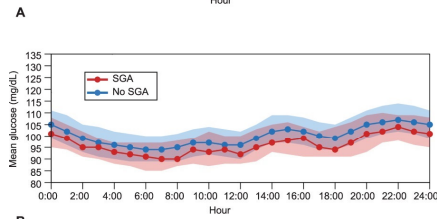
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CGMS on all patients



- N=760 , 7.2% with GDM
- % Time above 120mg/dL associated with increased risk of LGA and Hypertensive disorders.

“Even among those who were not diagnosed with GDM, the percent time above 120 mg/dL and above 140 mg/dL was higher in those with HDP than those without HDP (median time above 120 mg/dL: 15% vs 12%, P,.001; median time above 140 mg/dL: 3.3% vs 2.7%, P,.001)”



[Continuous Glucose Monitoring—Derived Differences in Pregnancies With and Without Adverse Perinatal Outcomes](#)

Durnwald, Celeste; Beck, Roy W.; Li, Zoey; Norton, Elizabeth; Bergenstal, Richard; Johnson, Mary; Dunnigan, Sean; Banfield, Matthew; Krumwiede, Katie; Sibayan, Judy; Calhoun, Peter; Carlson, Anders L.
 Obstetrics & Gynecology 144(5):684-696, November 2024.
 doi: 10.1097/AOG.0000000000005668

