AADE16

Embrace Change, Strengthen Our Future, Celebrate!

AADE American Association of Diabetes Educators

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- Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours

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- Presenter: Erin Raney, Pharm.D., BCPS, BC-ADM– No COI/Financial Relationship to disclose

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A Healthy Beginning: Diabetes and Preconception Health

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Learning Objectives

- Describe the importance of preconception health to maternal and infant morbidity and mortality
- Discuss preconception lifestyle recommendations for reproductive age women with diabetes
- List recommended preconception assessments for microvascular and macrovascular disease for women with diabetes
- Describe preconception medication strategies to optimize glycemic control and medication safety during pregnancy

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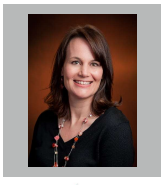

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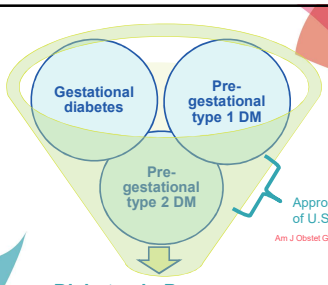

Diabetes in Pregnancy

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Pregnancy-Related Risks

Spontaneous abortion

Macrosomia

Fetal anomalies

Type 2 diabetes in offspring

Neonatal hypoglycemia

Preterm labor

Preeclampsia

Diabetes Care 2016;39(Suppl 1):S94-98.

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Preconception Care

"Preconception care is the provision of biomedical, behavioural and social health interventions to women and couples before conception occurs, aimed at improving their health status, and reducing behaviours and individual and environmental factors that could contribute to poor maternal and child health outcomes. Its ultimate aim is improved maternal and child health outcomes, in both the short and long term." (World Health Organization)

http://www.who.int/maternal_child_adolescent/documents/concensus_preconception_care/en/

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Diabetes Management

- **During pregnancy**
  - Tight glycemic control
    - Fasting ≤ 90 mg/dL, 1-hr postprandial ≤130-140 mg/dL, 2-hr postprandial ≤120 mg/dL
  - Medical nutrition therapy
  - Pharmacologic agents
    - Sulfonylureas, metformin, insulin for GDM
    - Insulin for pre-gestational type 1 and type 2 DM

Diabetes Care 2016;39(Suppl 1):S94-98.

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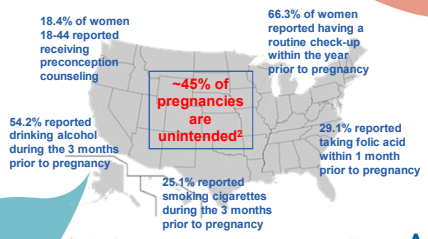
Preconception Health Indicators[1]



[1]CDC Core State Preconception Health Indicators 2009 MMWR 2014;63 (No.SS-3):1-62
[2]N Engl J Med 2016;374:843-52

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Preconception Counseling

What could we avoid EACH YEAR by providing preconception care for women with diabetes?

- 8397 preterm births
- 3725 birth defects
- 1872 perinatal deaths

Am J Obstet Gynecol 2015;212:74.e1-9

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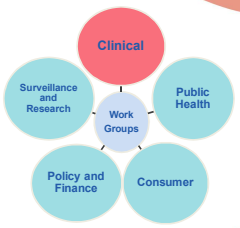
National Initiative on Preconception Health and Health Care (PCHHC)



http://www.cdc.gov/preconception/documents/ActionPlanNationalInitiativePCHHC2012-2014.pdf

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Clinical Toolkit

- National Preconception/ Interconception Clinical Toolkit
  - **"One Key Question:"** Would you like to become pregnant in the next year?
    - Women who desire pregnancy in the next year
    - Women who are ambivalent about pregnancy in the next year
    - Women who do not desire pregnancy in the next year

http://beforeandbeyond.org/toolkit/

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Nutrition Status

Diane has been trying to improve her dietary choices and sees a possible pregnancy as an additional incentive. She does not take any nutritional supplements and is lactose intolerant.

Vitamin D	Calcium	Iron
• 600 IU daily	• 1000 mg daily	• 15 mg daily (age 14-18) • 18 mg daily (age 19-50)

Fatty Acids	Iodine	Folic Acid
• 8-12 ounces of EFA containing seafood weekly • Avoid high mercury content	• 150 ug daily	• 400 mcg daily • High risk consider 4 mg daily

http://beforeandbeyond.org/toolkit/

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Case Study

Diane is a 32 year old woman with type 2 diabetes diagnosed at age 30. She has determined that she is interested in conceiving within the next 1-2 years. She would like to stop using contraception (she has had a levonorgestrel IUD placed for 4 years).

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Weight Management

Diane's BMI is now 29 kg/m^2. This is improved from 33 kg/m^{2}2 years ago. She finds it hard to exercise routinely due to her busy schedule.

Underweight BMI	Normal BMI	Overweight BMI	Obese BMI
• Assess risks for eating disorders • Review impact on preterm birth, low birth weight	• Encourage weight maintenance and physical activity	• Counsel on long term health risks • Encourage weight loss • Consider pregnancy risk with medications for weight loss	• Same as overweight BMI • Consider lower efficacy of certain contraceptives

http://beforeandbeyond.org/toolkit/

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Clinical Toolkit

- Nutrition Status
- Substance Use/Abuse
- Infectious Disease/Immunizations
- Chronic Diseases
- Medications
- Family Planning
- Previous Pregnancy Outcomes
- Genetic Risks
- Mental Health
- Interpersonal Violence

http://beforeandbeyond.org/toolkit/

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Substance Use/Exposures

- Discuss risks of alcohol, tobacco, and illicit drug use prior to pregnancy
  - No safe level of alcohol use during pregnancy (associated risk for fetal alcohol syndrome)
  - Pharmacologic tobacco cessation methods generally not recommended for use during pregnancy
  - Many illicit drugs associated with pregnancy risk and long-term child developmental dysfunction
- Assess for environmental and occupational exposures

Diane does not smoke but she does drink 2-3 alcoholic beverages 3-4 times per week. She denies illicit drug use. She works as a human resources manager for a retail clothing chain.

http://beforeandbeyond.org/toolkit/

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Immunizations and Pregnancy[1]

Avoid During Pregnancy	•MMR (avoid pregnancy for 1 month after vaccine) •Varicella/Zoster (avoid pregnancy for 1 month after vaccine) •Influenza LAIV •HPV
Give Only if Indicated	•Hepatitis A, Hepatitis B* •Meningococcal conjugate/polysaccharide •Pneumococcal polysaccharide* •Polio
Give During Pregnancy	•Influenza (IIV)* •Tdap

*Immunizations specifically recommended for patients with diabetes[2]

Diane received all childhood vaccines and her last Td booster was 7 years ago. She has never received hepatitis A or B vaccines. She has never had chicken pox and doesn't remember receiving the varicella or pneumococcal vaccines. She does not usually get a flu shot.

[1]http://www.cdc.gov/vaccines/pubs/preg-guide.htm
[2]Diabetes Care 2016;39(Suppl 1):S94-98.

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Medication Safety

- General approach
  - Review medications for pregnancy risk
  - Identify potentially safer alternatives, if possible
  - Recommend effective contraception methods if high risk medications used
  - If pregnancy desired, plan transition period for medications and optimize other factors associated with disease control

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Chronic Disease Management

- Recommended preconception diabetes assessments
  - Glucose control (A1C <6.5% recommended prior to pregnancy due to associated reduction in risk for congenital anomalies)
  - Renal function assessment (urinary albumin-to-creatinine ratio/serum creatinine)
  - Comprehensive eye exam
  - Assessment of thyroid function
  - HIV testing
  - Up-to-date Pap test

Diabetes Care 2016;39(Suppl 1):S94-98.

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Medication Safety

- Interpretation of pregnancy risk is complicated by available information
  - Limited clinical trial data
  - Oversimplification of risk with prior use of pregnancy letter categories
- Communication of risk prior to conception is also poor[1,2]
  - Studies indicate little attention given to contraception counseling for potentially teratogenic medications
  - ~50% of women receiving a prescription for a category D or X medication received contraceptive counseling

[1]Ann Intern Med 2007;147:370-376
[2]Med Care 2010;48:834-842

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Chronic Disease Management

- Diane has a physical exam and laboratory assessments:
  - Quarterly A1C for past year: 6.9%, 7.8%, 7.2%, 7.4% (most recent)
  - Blood pressure 128/82 mm/Hg (prior to medication 150/98)
  - Renal function
    - Serum creatinine 1.1 mg/dL
    - Urinary albumin-to-creatinine ratio 14 mg/g
  - FLP (TG 135 mg/dL, HDL 44 mg/dL, LDL 110 mg/dL)
  - Comprehensive eye exam WNL
  - TSH 2.95 (0.5-4.7 mIU/L)
  - HIV negative
  - Most recent Pap test negative 1 year ago

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Medication Safety

- Final Rule: Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling
  - Newly approved prescription drug products as of June 30, 2015 must comply with this rule
  - Previously approved products (since 2001) will be phased in over time
  - Letter categories will be removed from all products over time

http://federalregister.gov/a/2014-28241

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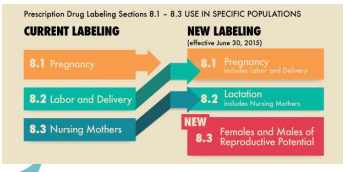
Medication Labeling

Subsections of 8.1 and 8.2 include "risk summary," "data," and "clinical considerations"



http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm

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Medication Safety

Non-insulin antidiabetics with the MOST safety data during pregnancy[1,2]

Medication	Considerations[2]
Metformin	Primarily studied for GDM in comparison with insulin[3] (appeared equal except higher risk for preterm birth)
Glyburide	Most clinical evidence from use in GDM Glipizide and glimepiride have greater evidence of placental transfer Recent study of glyburide identified hypoglycemia risk (and other adverse pregnancy outcomes) versus insulin[4]
Acarbose	*Human data more limited than with glyburide and metformin* *Less data available for miglitol (not recommended)*

[1]Diabetes Care 2016;39(Suppl 1):S94-98.
[2]Briggs' Drugs in Pregnancy and Lactation. Accessed at Facts and Comparisons eAnswers online.factsandcomparisons.com
[3]N Engl J Med 2008;358:2003-15
[4]JAMA Pediatr 2015;169:452-8

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Medication Safety

Diane's medications include:
Metformin 1000 mg BID
Sitagliptin 100 mg once daily
Lisinopril 5 mg once daily

- Diabetes-related medications
  - Glucose control
    - Insulin
    - Non-insulin antidiabetic medications
  - Blood pressure management and renal protection
    - Antihypertensives
  - Lipid management
    - Statins
    - Other antihyperlipidemics

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Medication Safety

Non-insulin antidiabetics NOT recommended during pregnancy

Medication Class	Considerations
GLP-1 agonists	Limited human data/malformations in animal studies
DPP-4 inhibitors	No human data/limited risk shown in animal studies
SGLT-2 inhibitors	No human data/renal malformations in animal studies
Thiazolidenediones	Limited human data/adverse pregnancy outcomes in animal studies
Meglitinides	Limited human data/limited risk in animal studies
Amylin mimetics	Limited human data/malformations in animal studies

Briggs' Drugs in Pregnancy and Lactation. Accessed at Facts and Comparisons eAnswers online.factsandcomparisons.com

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Medication Safety

- Insulin considered gold standard for treating DM during pregnancy
  - Safety of regular and NPH insulin well established in clinical studies
  - Experience with insulin lispro, insulin aspart, and insulin detemir appears positive
  - Limited information available in humans on other insulin analogs in pregnancy

Diabetes Care 2016;39(Suppl 1):S94-98
Arch Gynecol Obstet 2015;292:749-56

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Medication Safety

- Antihypertensives
  - Medications recommended for treatment of hypertension in people with diabetes Diabetes Care 2016;39(Suppl 1):S1-119.
    - ACE inhibitors/angiotensin receptor blockers
    - Calcium channel blockers
    - Diuretics
  - Medications recommended for treatment of hypertension during pregnancy (general use) Obstet Gynecol 2013;122:1122-1131
    - Methyldopa
    - Labetalol
    - Nifedipine

Clinical dilemma

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Medication Safety

Select Medication Classed	Considerations in Pregnancy with DM
ACE inhibitors/ ARBs/direct renin inhibitors	CONTRAINDICATED (Category X in prior pregnancy risk format) Evidence of renal malformations, oligohydramnios, fetal growth restriction
Diuretics	Thiazides typically avoided due to risk for reduced placental perfusion Spironolactone CONTRAINDICATED due to antiandrogen effects

Obstet Gynecol 2013;122:1122-1131

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Medication Safety

- Non-statin antihyperlipidemics in pregnancy[1]
  - Limited information on safety of bile acid resins, omega-3 fatty acids, niacin, ezetimibe during pregnancy
  - Limited human safety data for fibrates, but animal data indicate possible risk
- General approach in women of reproductive potential
  - Statins appropriate with the use of effective contraception
  - Colesevelam may be an option for women of childbearing age who require treatment but are not appropriate candidates for a statin (not able/willing to use effective contraception)[2]

[1]Briggs' Drugs in Pregnancy and Lactation. Accessed at Facts and Comparisons eAnswers online.factsandcomparisons.com
[2]J Clin Lipidol 2012;6:88-91

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Medication Safety

- Antihyperlipidemics
  - Use of statin therapy is first-line agent supported for use in non-pregnant patients with diabetes

Age	Recommendation
< 40 years with ASCVD or risk factors (LDL ≥100, HTN, smoking, overweight/obesity, family history of premature ASCVD)	Moderate to high intensity statin (consider use for ASCVD risk factors/high intensity for ASCVD)
40-75 years	Moderate to high intensity statin (high intensity for those with ASCVD/risk factors)

Diabetes Care 2016;39(Suppl 1):S1-119.

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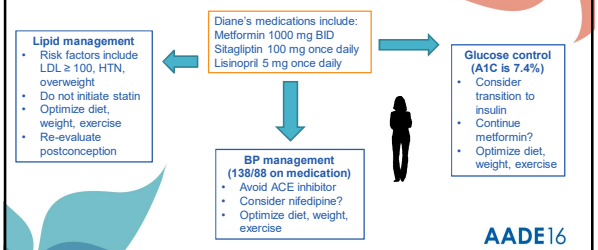
Medication Transition Plan



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Medication Safety

- Antihyperlipidemics
  - Drug treatment for dyslipidemia during pregnancy is typically limited to specific populations
    - Cholesterol required for fetal development
    - Short term exposure to medications may impose a higher risk than any cardiovascular benefit gained
      - Statins contraindicated during pregnancy due to teratogenicity[1,2]
        - » Category X in prior pregnancy risk format
        - » Various malformations reported from use of lipophilic statins (analysis showed risk rate similar to general population)[2,3]

[1]Diabetes Care 2016;39(Suppl 1):S1-119.
[2]Briggs' Drugs in Pregnancy and Lactation. Accessed at Facts and Comparisons eAnswers online.factsandcomparisons.com
[3]Birth Defects Res A Clin Mol Teratol 2005;73:888-96

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Family Planning

- Discuss development of a "reproductive life plan"
  - Set of personal goals about having or not having children, including a plan on how to achieve those goals based upon personal beliefs (marriage, abstinence, use of pharmacologic contraception, etc…)

http://www.cdc.gov/preconception/documents/reproductivelifeplan-worksheet.pdf
http://www.cdc.gov/preconception/documents/rlphealthproviders.pdf

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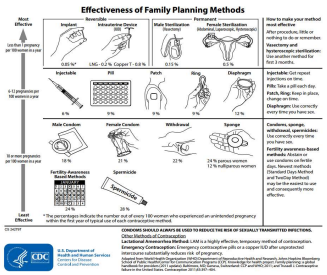
Family Planning



http://www.cdc.gov/reproductivehealth/unintendedpregnancy/pdf/contraceptive_methods_508.pdf

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Summary

- Preconception care is appropriate to provide at all clinical visits with women of reproductive potential (not only for women planning pregnancy)
- Optimization of lifestyle factors, immunizations, and medication risks prior to pregnancy positively impacts pregnancy outcomes
- Reproductive life plans can enable women with diabetes to time pregnancy once maximal glycemic control and management of macrovascular and microvascular risk has been achieved

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Contraception and Diabetes

Medical eligibility criteria for contraceptives in women with diabetes

DM Condition	CHC (initiation/ continuation)	POP	INJ	IMP	LNG-IUD	Cu-IUD
History of GDM	1	1	1	1	1	1
Non-vascular disease	2	2	2	2	2	1
Nephropathy/neuropathy /retinopathy	3/4	2	3	2	2	1
Other vascular disease	3/4	2	3	2	2	1
DM > 20 years	3/4	2	3	2	2	1

CHC=combined hormonal contraceptive
POP=progestin-only pill
INJ=depomedroxyprogesterone injection
IMP=etonogestrel subdermal implant
LNG-IUD=levonorgestrel IUD
Cu-IUD=copper IUD

http://www.cdc.gov/mmwr/pdf/rr/rr5904.pdf

1=no restriction
2=advantages of method generally outweigh risks
3=risks of method generally outweigh advantages
4=do not use

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Additional Resources

- Centers for Disease Control and Prevention (CDC). Recommendations to improve preconception health and health care—United States. MMWR Recommendations and Reports. 2006;55(RR-06):1–23.
- Jack BW, Atrash HK, Coonrod DV, et al. The clinical content of preconception care: an overview and preparation of this supplement. Am J Obstet Gynecol 2008;199 (Suppl 2):S266-279.
- Before, Between and Beyond Pregnancy http://beforeandbeyond.org/
- CDC http://www.cdc.gov/preconception/index.html
- CDC "Show Your Love" Campaign http://www.cdc.gov/preconception/showyourlove/index.html

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Contraception

- Considerations
  - Hormone-based methods are often the most effective reversible option when high risk medications are used or if glycemic control needs improvement before pregnancy
  - If macrovascular or microvascular disease is present, certain progestin-only methods are preferred (or copper IUD)
    - Blood pressure considerations are important with estrogen-containing products
  - Weight considerations
    - Obesity affects the pharmacokinetics of hormonal contraceptives, but efficacy is not clearly impacted with most options (reduced efficacy with the contraceptive patch (>90 kg))
    - Weight gain caused by contraceptives is often a concern; injectable medroxyprogesterone acetate and the copper IUD appear to be most associated

Obstet Gynecol Clin N Am 2015;42:647-57

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