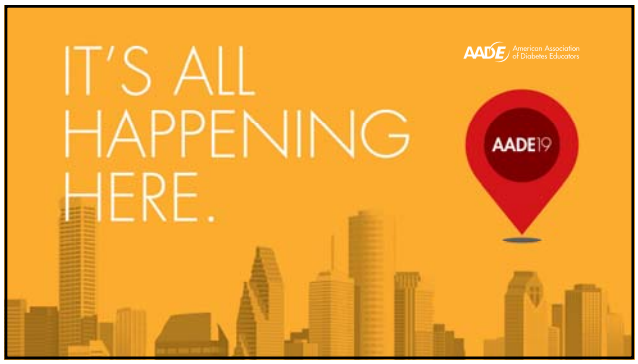

1

Type 1 Diabetes in Women: from Menarche to Menopause

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Disclosure to Participants

- Notice of Requirements For Successful Completion
  - Please refer to learning goals and objectives
  - Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours
- Conflict of Interest (COI) and Financial Relationship Disclosures:
  - Presenter: Eileen Egan- No COI/Financial Relationship to disclose
  - Presenter: Audrey LaVigne- No COI/Financial Relationship to disclose
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Learning Objectives

- Identify at least 3 health challenges faced by women with Type 1 diabetes
- Describe at least 3 strategies the diabetes educator can employ to assist women with Type 1 diabetes overcome these challenges
- Compare statistics regarding at least 3 of these health challenges between women without diabetes as well as men with men who have type 1 diabetes

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Women with T1 DM

- ~1.25 million Americans living with T1 DM
  - ~193,000 under the age of 20
  - ~40,000 new diagnoses annually
  - Average age at diagnosis is 8-10 years
  - Fairly equal rates of diagnosis between girls and boys
- Psychologic and physiologic burden higher for women
  - Less likely to achieve A1C < 7%
  - Higher rates of nocturnal hypoglycemia
  - More likely to have anxiety and depression

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Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services, 2017.

6

Meet Sienna

- Sienna is a 14 year old girl diagnosed with type 1 diabetes at the age of 8
  - She presents to your office for follow up diabetes education
  - Sienna reports she got her first period last week
  - She states her numbers have been "crazy" since her last appointment 2 months ago
  - She is accompanied by her mother

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Common Issues During Puberty

- Excessive weight gain or weight loss
  - Often related to hormonal changes & body image
- Difficult to regulate glucose
  - Often related to hormonal changes; growth & development
- Struggles with self-management
  - Prioritizing DM

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Puberty

- Young women with Type 1 typically experience
  - Later menarche
  - Fewer pregnancies
  - Increased stillbirths
- Two-fold increase in menstrual problems before age 30
  - Longer cycles
  - Heavy menstruation

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Schweiger, et al (2011) Menarche delay and menstrual irregularities persist in adolescents with type 1 diabetes. Reproductive Biology and Endocrinology. 9(61):6-8

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Menarche

- Typically delayed for women with T1 DM
  - Girls diagnosed with T1 DM before age 10 years had a significant delay in menses
  - Girls with T1 DM diagnosed after age 10 years had less of a delay
- Potential causes
  - Period of weight loss and physiologic stress prior to diagnosis
  - Chronic disease typically associated with menses delay
  - Weight loss associated with altered metabolism

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Schweiger, et al (2011) Menarche delay and menstrual irregularities persist in adolescents with type 1 diabetes. Reproductive Biology and Endocrinology. 9(61):6-8
Strotmeyer, et al (2003) Menstrual cycle differences between women with type 1 diabetes and women without diabetes. Diabetes Care/American Diabetes Association

10

Age of Menarche in T1 DM Compared to General Population

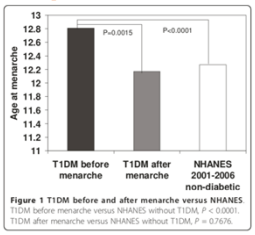

Figure 1 T1DM before and after menarche versus NHANES
T1DM before menarche versus NHANES without T1DM, $P < 0.0001$.
T1DM after menarche versus NHANES without T1DM, $P = 0.7676$.

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Schweiger, et al (2011) Menarche delay and menstrual irregularities persist in adolescents with type 1 diabetes. Reproductive Biology and Endocrinology. 9(61):6-8

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Menarche

- Age of menarche negatively associated with BMI
  - Higher BMI associated with earlier menses
- Level of A1C not associated with delayed menarche
- Despite improvement in diabetes treatment, menarche delay and menstrual irregularity continue to be a concern among women with T1 DM
- Women diagnosed after menarche do not seem to be impacted by these irregularities

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Schweiger, et al (2011) Menarche delay and menstrual irregularities persist in adolescents with type 1 diabetes. Reproductive Biology and Endocrinology. 9(61):6-8

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Menses

- Characteristics of T1 DM menstrual cycle differs by age
  - Age < 20 & 20-29 years
    - duration typically > 6 days
    - Heavy menstruation
    - Cycle > 31 days
  - Age 30-49 years
    - No significant difference among women with T1 DM compared to women without DM

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Strotmeyer, et al (2003) Menstrual cycle differences between women with type 1 diabetes and women without diabetes. Diabetes Care/American Diabetes Association

13

Polycystic Ovarian Syndrome

- Most common endocrine disorder among women of child bearing age
  - Prevalence in women with T1 DM ~24%
  - Prevalence in general population ~6-15%
- Most common cause of anovulation
- Symptoms include
  - Oligomenorrhoea
  - Elevated androgen levels
  - Hirsutism and acne
  - Decreased fertility

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Escobar-Morreale, et al (2016). Type 1 diabetes and polycystic ovarian syndrome: systematic review and meta-analysis. Diabetes Care. 39: 639-648

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Collaborating with the Diabetes Educator

- Gain trust in order to establish a working relationship
- Shared decision making rather than interventions
- Establish patient centered goals, allowing her to prioritize what is most important

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What's in the Toolbox?

- Basal adjustments for hormonal variations
- Educate on growth and development and the impact on T1 DM
  - Taking ownership of self care
  - Hormonal fluctuations
  - Psychological impact
  - Insulin resistance
- Discuss treatment options: pump, CGM
- Increase touch points in between visits

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Sienna

- Sienna is struggling
  - She is now 18 y/o
  - Her A1C is 10% and has been >9% for the past few years
    - She admits to not checking routinely & omitting insulin doses
  - Her microalbumin creatinine ratio is elevated (confirmed x 2)
  - Her period is irregular
  - She has a boyfriend
    - Her mom is worried and thinks she has been drinking
    - She smells cigarette smoke on her clothing

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Sex, Drugs and Rock & Roll

- Late teens into 20s begins another struggle for control
  - Emerging adulthood
- Often the time when many young women drift and wander
- Often only communicating with health care team in time of crisis or when in need of prescriptions

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Sex, Drugs and Rock and Roll

- Body image disturbances
- Increased independence
  - Social, self care, financial
- Access to drugs and alcohol
- Increased sexual experimentation
- Psychological impact
  - Anxiety, depression

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Behavioral Disorders & Addiction

- Anxiety and depression
  - Self care burden
  - Glycemic control directly related
  - Chronic disease increased risk for depression
- Addiction issues
  - Dangerous in the presence of insulin

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Eating Disorders

- Adolescents and young women with T1 DM are at high risk
  - Pressure of constant food "restriction"
  - Weight management
  - Altered body image
  - Control issues
- Incidence
  - Pre-adolescence: 2%
  - Adolescence: 11-15 %
  - Young women: 30-39%

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Klinik, et al (2017) Diabulimia, a type 1 diabetes specific eating disorder. Turkish Archives of Pediatrics, 52(1):46-49

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Eating Disorders

- Diabulimia
  - Term to define when a person restricts or omits insulin in order to control weight
    - Calorie Purging as a results of insulin restriction
  - Once appropriate insulin dosing is resumed, weight re-gain occurs
    - The cycle then re-starts
- Anorexia
  - Increased risk for hypoglycemia

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Cheivanayagam, et al (2018) What is diabulimia and what are the implications for practice. British Journal of Nursing, 27(17):980-986

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Collaborating with the Diabetes Educator

- Remain supportive rather than judgmental
- Motivational interviewing
  - Employ open ended questions
- Address safe alcohol consumption versus binging
- Impact of drugs and alcohol on glucose
  - Hypoglycemia, DKA
- Smoking
  - Cigarettes, juules

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What's in the Toolbox?

- Depression/emotional issues
  - Open ended statements- weight/appearance changes
  - Networking with peers with T1DM
- Discuss options for contraception
  - Progesterone, estrogen, abstinence
- Ask about weekend plans

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Sienna

- Sienna is now 26 y/o
  - She got married last year and wants to start a family
  - Her A1C is 7.9%
  - She is on basal/bolus
  - She remains on oral contraception and an ACE inhibitor
  - She continues to smoke

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Pregnancy

- Pre-conception counseling & planning
  - Associated with better outcomes
  - Preconception A1C target < 6.5%
- Women with T1DM have higher rates of
  - Miscarriage, pre-eclampsia, pre-term delivery, c-section, mortality
    - Increased risk for retinopathy & nephropathy
- Neonates have higher rates of
  - Hypoglycemia, macrosomia, weight abnormalities, congenital malformations

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American Diabetes Association (2019). Management of diabetes in pregnancy: standards of medical care in diabetes- 2019. Diabetes Care. Suppl. 1:S165-S172.
Ludvigsson, et al. (2019). Maternal glycemic control in type 1 diabetes and the risk for preterm birth. Ann of Intern Med. April 23. doi: 10.7326/M18-1974.

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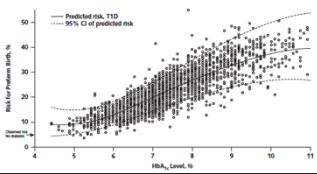
Pregnancy: risk of pre-term birth

Table 2. Association Between T1D and Risk for Preterm Birth, by HbA_{1c} Level in the Periconceptional Period

Outcome Measures	No Diabetes	T1D Overall	T1D, by HbA_{1c} Level			
			<6.5%	6.5% to <7.8%	7.8% to <9.1%	≥9.1%
Preterm birth						
Infants, *n*	1 165 216	2474	555	1127	544	248
Events, *n* (%)	54 287 (4.7)	552 (22.3)	73 (13.2)	232 (20.6)	154 (28.3)	93 (37.5)



Ludvigsson, et al. (2019). Maternal glycemic control in type 1 diabetes and the risk for preterm birth. Ann of Intern Med. April 23. doi: 10.7326/M18-1974.

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Pregnancy: risk for adverse outcomes

Figure 4. Association between T1D and risk for secondary adverse pregnancy outcomes, by HbA_{1c} levels.

Outcome, by HbA_{1c} Level	Infants, *n*	Events, *n* (%)	aRR (95% CI)*
LGA			
No diabetes	1 163 085	38 058 (3.3)	–
<6.5%	547	140 (25.6)	7.75 (6.72–8.95)
6.5% to <7.8%	1089	441 (40.5)	11.22 (10.37–12.14)
7.8% to <9.1%	519	251 (48.4)	12.88 (11.69–14.20)
≥9.1%	238	95 (39.9)	12.01 (10.23–14.09)
Macrosomia†			
No diabetes	1 109 502	41 799 (3.8)	–
<6.5%	480	54 (11.3)	2.88 (2.23–3.72)
6.5% to <7.8%	890	174 (19.6)	4.65 (4.06–5.32)
7.8% to <9.1%	388	96 (24.7)	5. 76 (4.85–6.85)
≥9.1%	155	26 (16.8)	4.36 (3.14–6.07)
Hypoglycemia			
No diabetes	1 165 216	25 168 (2.2)	–
<6.5%	555	135 (24.3)	11.30 (9.73–13.12)
6.5% to <7.8%	1127	402 (35.7)	15.45 (14.21–16.80)
7.8% to <9.1%	544	207 (38.1)	16.21 (14.43–18.22)
≥9.1%	248	97 (39.1)	16.03 (13.55–18.96)

Ludvigsson, et al. (2019). Maternal glycemic control in type 1 diabetes and the risk for preterm birth. Ann of Intern Med. April 23. doi: 10.7326/M18-1974.

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Pregnancy Glycemic Targets

A1C

- A1C
  - < 6-6.5%
  - Looser target if hypoglycemia risk is great
  - Rely more on daily glucose checking due to increased red blood cell turnover

Daily

- Blood Glucose
  - Fasting < 95 mg/dl
  - 1 hour post prandial < 140 mg/dl
  - 2 hour post prandial < 120 mg/dl

American Diabetes Association (2019). Management of diabetes in pregnancy: standards of medical care in diabetes- 2019. Diabetes Care. Suppl. 1:S165-S172.

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Preconception Collaboration with the Diabetes Educator

- A1C target
  - ≤ 6.5%
- Insulin delivery
  - consider a pump and a CGM
- Other medications
  - Stop all potentially teratogenic medications; the ACE-i
- Smoking cessation
- Other screenings
  - Dilated eye exam
  - Dietitian
  - Labs

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Pregnancy Challenges: what's in the Toolbox?

Challenges

- 1st trimester
  - Nausea and vomiting
  - Hypoglycemia
- 2nd trimester
  - Insulin resistance
  - Weight gain
- 3rd trimester
  - Hypertension, pre-eclampsia
  - Insulin sensitivity in the few weeks preceding delivery

Collaborative Plan

- 1st trimester
  - Micro boluses
  - Review use of glucagon
- 2nd trimester
  - Frequent increases in insulin, especially carb ratios
  - Follow up with the RD
- 3rd trimester
  - Use of labetalol for BP, aspirin 81 mg
  - Potential need for insulin dose reductions

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Postpartum Challenges: what's in the Toolbox?

Challenges

- Increased insulin sensitivity immediately after delivery
- Hypoglycemia related to breastfeeding
- Glycemic variability related to sleep deprivation and remembering to bolus

Collaborative plan

- Reduce insulin doses
  - ~75% reduction in insulin
  - Set up a basal profile
- Snacking prior to breastfeeding
  - Snack; no bolus
  - Meal; reduced bolus ~25%
- Ask for help
  - Family, friends
  - Reminders on phone
  - Smart technology

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Sienna

- Two successful pregnancies
  - Resumed smoking
- Now 45 y/o
  - Fractured her foot last year; tripped over the curb
- Busy working mom
  - A1C 7.3%
  - BMI 29, waist circumference 37
  - BP 148/90
  - LDL 130
  - Mild background diabetic retinopathy & diabetic nephropathy
  - Irregular menses, night sweats

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Cardiovascular Disease in T1 DM

- Rates of CVD (coronary heart disease and peripheral arterial disease) are ~ 10 x higher than the general population
  - Increased endothelial dysfunction
  - Increased inflammatory markers
    - Acute hypoglycemia and hyperglycemia are associated with complex vascular events leading to inflammation
  - Increased coronary artery calcification
    - Associated with atherosclerosis

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deFerranti, et al. (2014) Type 1 diabetes and cardiovascular disease, a scientific statement form the American heart association and the American diabetes association. Circulation. 130:1110-1130.

34

Cardiovascular Disease in T1 DM

- Heart disease occurs 10-15 years earlier than in the general population, but disease generally more advanced by the time of diagnosis
  - Impact of cardiovascular autonomic neuropathy; may affect up to 40% of people with T1 DM
    - Impaired heart rate variability
    - Orthostatic hypotension
    - Exercise intolerance

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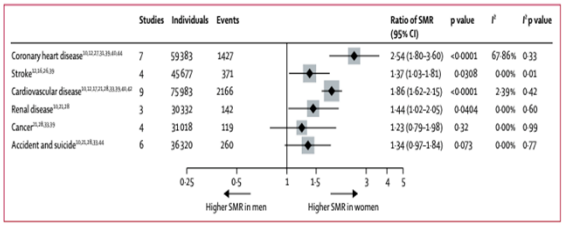
deFerranti, et al. (2014) Type 1 diabetes and cardiovascular disease, a scientific statement form the American heart association and the American diabetes association. Circulation. 130:1110-1130.

35

Cardiovascular Disease T1 DM: Men vs. Women



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Huxley, et al. (2015). Risk of all-cause mortality and vascular events in women versus men with type 1 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinology. 3(3): 198-206

36

Cardiovascular disease in T1 DM Women

- Young adult women with T1 DM
  - Develop CVD earlier than age-matched women without DM
  - Are at higher risk of CVD than male counterparts with T1 DM
- Duration of DM >15 years is associated with higher mortality in women with CVD
- In general women with T1 DM
  - are at greater risk for mortality related to CVD and renal disease then men with T1 DM
  - Have 2 x higher risk of vascular events then men with T1 DM

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deFerranti, et al. (2014). Type 1 diabetes and cardiovascular disease, a scientific statement form the American heart association and the American diabetes association. Circulation. 130:1110-1130.
Huxley, et al. (2015). Risk of all-cause mortality and vascular events in women versus men with type 1 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinology. 3(3): 198-206.

37

Cardiovascular Disease in T1 DM Women

- Women often experience atypical symptoms
  - Nausea, reflux, abdominal pain
- Women are often dismissed and thought to have anxiety
  - Higher rates of macrovascular disease than male counterparts
  - Higher rates of all cause mortality, especially young adult women

#AADE19

deFerranti, et al. (2014) Type 1 diabetes and cardiovascular disease, a scientific statement form the American heart association and the American diabetes association. Circulation. 130:1110-1130.
Maric-Bilkan (2017). Sex differences in micro and macro-vascular complications of diabetes mellitus. Clinical Science. 131(9): 833-846.

38

Urological Complications

- 65% of women repot at least 1 urological complication
- Female Sexual Dysfunction
  - Associated with psychological variables, chronic disease management, poor glycemic regulation; lead to depression and dysfunction
  - Affects ~42% of women with T1 DM
  - Often overlooked in women
    - Embarrassment, body image issues
- Urinary Tract Infections and Urinary Incontinence
  - Impacts ~17% and 31% of women with T1 DM respectively
  - Can result in significant hyperglycemia
  - Asymptomatic, propensity for diabetic ketoacidosis

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Wessels, et al. (2018) Burden of Urologic complications in men and women with long-standing type 1 diabetes in the diabetes control and complications trial/epidemiology of diabetes interventions and complications cohort. Diabetes Care. 41: 1670-1678.

39

Menopause

- Age of menopause
  - Conflicting data
    - Presence of microvascular complications my be associated with earlier menopause, otherwise no different than women without diabetes
  - Fewer fertile years
- Symptoms of menopause
  - May overlap with symptoms of hypoglycemia & autonomic neuropathy
- Treatment of menopause
  - consider HRT on an individual basis

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Yarde, et al. (2015) Age at menopause in women with type 1 diabetes: the OVADIA study. Hum Reprod. 30 (2): 441-446.
Morling, et al. (2013). Diabetes in women- a life course approach. Menopause International. 19(2): 87-95

40

Collaborating with the Diabetes Educator

- Optimize A1C, BP and lipids to mitigate progression of microvascular complications
  - Weight management & exercise
  - Escalate ACE-i, may need 2nd agent
- Smoking cessation counseling at every visit
- CVD
  - Statin therapy; high intensity, assess adherence
  - Assess for cardiovascular autonomic neuropathy
- Menopause
  - HRT? (not if still smoking)
  - Ability to differentiate symptoms of hypoglycemia, impact on quality of life

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Sienna

- Now 65 years old
- Microvascular complications
  - Retinopathy and nephropathy: stable
- Hyperlipidemia
  - Controlled, on a high intensity statin
- Hypertension
  - Controlled, on an ACE-i
- First DEXA
  - Osteopenia of the hip
  - FRAX score: 3% for hip, 20% for major osteoporotic fractures
    - Personal history of fracture, smoker, mother with history of hip fracture

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Osteoporosis

- Often considered a complication of T1 DM
  - ~ 50% of T1 DM have bone loss
  - ~ 20% aged 20-56 have osteoporosis
- Lower BMD
  - Impact of hyperglycemia & microvascular complications
  - Duration of DM
  - A1C
- Higher rates of hip fracture
  - 12 x higher risk
    - Associated with microvascular complications

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Morling, et al. (2013). Diabetes in women- a life course approach. Menopause International. 19(2); 87-95.
Loannie, et al. (2019) Risk for fragility fractures in type 1 diabetes. Bone. April 17 2019. doi.org/10.1016/j.bone.2019.04.017

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Collaborating with the Diabetes Educator

- Osteoporosis
  - Dietary intake of calcium & vitamin D
  - Regular exercise
    - In particular strength training and weight bearing
  - Safety mechanisms for fall prevention
  - Screening with DEXA every 2 years
  - Medication therapy
    - Bisphosphonate, estrogen, denosumab, teriparatide

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Sienna……..success

- Retires to Boca
- Lives out the rest of her life, happy and healthy
  - Thanks to continued guidance from a Diabetes Educator !!!

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45

References

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