#### **ADVANCED TRACK**

# PROTECTING BONES AND BRAINS: DIABETES AND THE BRAIN

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# **Fracture Risk in Diabetes**

# Type 1 diabetes and risk of fracture: meta-analysis and review of the literature

V. N. Shah<sup>1</sup>, C. S. Shah<sup>2</sup> and J. K. Snell-Bergeon<sup>1</sup>

- 27,300 patients with type 1 diabetes
- 4,364,125 controls without diabetes

Osteoporos Int (2017) 28:3113-3121 DOI 10.1007/s00198-017-4183-0

ORIGINAL ARTICLE

#### Risk of low-energy fracture in type 2 diabetes patients: a meta-analysis of observational studies

P. Jia<sup>1</sup> · L. Bao<sup>1</sup> · H. Chen<sup>1</sup> · J. Yuan<sup>2</sup> · W. Liu<sup>2</sup> · F. Feng<sup>1</sup> · J. Li<sup>1</sup> · H. Tang<sup>1</sup>

- 272,717 patients with type 2 diabetes
- 666,025 controls without diabetes

Fracture risk is 20-30% higher in people with type 2 diabetes

Fracture risk is 300-400% higher in people with type 1 diabetes



#### FRACTURE RISK BY AGE AND SEX IN T1D



JBMR 2014; 29: 1054-1060

#### WHY FRACTURE RISK IS HIGH IN DIABETES?

# Bone Mineral Density



# **Bone Quality**



# **Frequent Falls**





Shah VN, DiMeglio L. Chapter 23# Sweet Bones: effect of diabetes on bone. Basics and Applied Bone Biology, 2<sup>nd</sup> edition

## WHAT YOU CAN DO TO KEEP YOUR BONES HEALTHY?

- 1. Be aware of this complication
- 2. Speak with your doctor for osteoporosis screening
- 3. Have adequate calcium and vitamin D in diet. Taking more than required calcium or vitamin D is not helpful
- 4. Regular exercise to improve strength and balance
- 5. Fall assessment and Prevention





Stepping On is a program that has been researched and proven to reduce falls in older people.

#### WHAT YOU CAN DO TO KEEP YOUR BONES HEALTHY?

6. Have optimal blood sugar control from the early onset of diabetes

7. Take medication if you are diagnosed with osteoporosis to help prevent further bone loss

8. Take part in research so that we can learn and treat this condition better



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#### I have no conflicts of interest to disclose.



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- As diabetes treatments advance, people are "...surviving and thriving into their later decades."
- We are learning more about T1D and issues associated with aging.
- 1. Image: Christina Kalberg, "Next Stop a Cure? A Quick History of Diabetes Research", beyondtype1.org
- 2. ElSayed NA, et al. Older Adults: Standards of Care in Diabetes 2023. *Diabetes Care*. 2023.



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1. Sachdev PS, et al. Classifying neurocognitive disorders: the DSM-5 approach. Nat Rev Neurol. 2014.



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### **DIABETES & THE BRAIN**

- Differences in brain structure.
- Lower cognitive performance scores.
  - IQ typically in normal range.
- Increased rates of cognitive impairment and dementias in older age.
  - "Accelerated brain aging".
- Diabetes and depression negatively impact cognition in a collaborative way.
- <u>Cognitive functioning may impact home diabetes management.</u>
- 1. ElSayed NA, et al. Older Adults: Standards of Care in Diabetes 2023. *Diabetes Care*. 2023.
- 2. Xue, et al. Diabetes mellitus and risks of cognitive impairment and dementia: A systematic review and meta-analysis. Ageing Research Reviews. 2019.
- 3. Schwartz, et al. Neurocognitive outcomes in pediatric diabetes: A developmental perspective. Curr Diab Rep. 2014.
- 4. Jacobson AM, et al. Cognitive performance declines in older adults with T1D: results from 32 years of follow-up in DCCT/EDIC. Lancet Diabetes Endo. 2021.



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#### THE LANCET Diabetes & Endocrinology



Volume 9, Issue 7, July 2021, Pages 436-445

Articles

Cognitive performance declines in older adults with type 1 diabetes: results from 32 years of follow-up in the DCCT and EDIC Study



#### **Associated Factors:**

- Higher A1c trends
  - 1 % increase = 3.3 years of aging
- History of severe hypoglycemia
  - 1+ event = 4.6 years of aging
- Higher systolic blood pressure
  - 5 point increase = 4.0 years of aging
- Other diabetes-related complications
  - Kidney disease
  - Eye disease
  - Cardiovascular disease

"...proportion of participants who met criterion for mild cognitive impairment was quite low (5.5%, n=58)."

Jacobson AM, et al. Cognitive performance declines in older adults with T1D: results from 32 years of follow-up in DCCT/EDIC. *Lancet Diabetes Endo*. 2021.

- Glucose and A1c trends
  - Lower A1cs / Higher time in range (TIR)
  - Avoid glycemic extremes

Article

https://doi.org/10.1038/s41467-022-32289->

A Pilot randomized trial to examine effects of a hybrid closed-loop insulin delivery system on neurodevelopmental and cognitive outcomes in adolescents with type 1 diabetes



- 1. Reiss AL, et al; Diabetes Research in Children Network (DirecNet) Consortium. A Pilot randomized trial to examine effects of a hybrid closed-loop insulin delivery system on neurodevelopmental and cognitive outcomes in adolescents with type 1 diabetes. *Nat Commun.* 2022.
- 2. ElSayed NA, et al. Older Adults: Standards of Care in Diabetes 2023. Diabetes Care. 2023.
- 3. Jaser SS, et al. Brain Health in Children with Type 1 Diabetes: Risk and Protective Factors. Curr Diab Rep. 2021.

- Prevent diabetic ketoacidosis (DKA)
  - Check ketones if ill, hyperglycemia
  - Insulin doses
  - Drink fluids
  - Balanced diet
- Reduce insulin resistance
  - Regular exercise



Some of the changes noted in skeletal muscle in response to exercise.

- 1. Image: Society for Endocrinology
- 2. Aye T, et al; Diabetes Research in Children Network (DirecNet) Study Group. Impact of Early DKA on the Developing Brain. Diabetes Care. 2019.
- 3. ElSayed NA, et al. Older Adults: Standards of Care in Diabetes 2023. Diabetes Care. 2023.



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- Prevent / manage micro- and macrovascular complications related to diabetes
  - Blood pressure
  - Cholesterol
- Prevent / address diabetes burnout, mental health
  - Show grace
  - One step at a time
  - Ask for help
  - Talk to your doctor
- 1. Image: beyondtype1.org
- 2. Musen G, et al. Cognitive Function Deficits Associated With Long-Duration Type 1 Diabetes and Vascular Complications. *Diabetes Care*. 2018
- 3. Jaser SS, et al. Brain Health in Children with Type 1 Diabetes: Risk and Protective Factors. *Curr Diab Rep.* 2021.



#### Talk to your doctor

- International Society for Pediatric and Adolescent Diabetes (ISPAD):
  - Psychosocial health should be monitored, and psychosocial care should be integrated in clinical practice.
  - Cognitive capacity and school functioning should be monitored.
- American Diabetes Association (ADA):
  - Screening for early detection of mild cognitive impairment or dementia should be performed for adults >65
    years at least yearly
  - Cognitive dysfunction makes it difficult for individuals to perform self-care tasks, maintain timing of meals and diet content... it is critical to simplify care plans and engage support.
- 1. ElSayed NA, et al. Older Adults: Standards of Care in Diabetes 2023. *Diabetes Care*. 2023.
- 2. de Wit M, et al. ISPAD Clinical Practice Consensus Guidelines: Psychological care of children, adolescents, young adults with diabetes. *Pediatr Diab*. 2022.



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#### REFERENCES

- 1. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, Kahan S, Khunti K, Leon J, Lyons SK, Perry ML, Prahalad P, Pratley RE, Jeffrie Seley J, Stanton RC, Gabbay RA, on behalf of the American Diabetes Association. 13. Older Adults: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023 Jan 1;46(Suppl 1):S216-S229. doi: 10.2337/dc23-S013. PMID: 36507638; PMCID: PMC9810468.
- 2. Sachdev PS, Blacker D, Blazer DG, Ganguli M, Jeste DV, Paulsen JS, Petersen RC. Classifying neurocognitive disorders: the DSM-5 approach. *Nat Rev Neurol*. 2014 Nov;10(11):634-42. doi: 10.1038/nrneurol.2014.181. Epub 2014 Sep 30. PMID: 25266297.
- 3. Xue M, Xu W, Ou YN, Cao XP, Tan MS, Tan L, Yu JT. Diabetes mellitus and risks of cognitive impairment and dementia: A systematic review and meta-analysis of 144 prospective studies. *Ageing Res Rev.* 2019 Nov;55:100944. doi: 10.1016/j.arr.2019.100944. Epub 2019 Aug 17. PMID: 31430566.
- 4. Schwartz DD, Wasserman R, Powell PW, Axelrad ME. Neurocognitive outcomes in pediatric diabetes: a developmental perspective. *Curr Diab Rep.* 2014 Oct;14(10):533. doi: 10.1007/s11892-014-0533-x. PMID: 25142718; PMCID: PMC4864497.
- 5. Jacobson AM, Ryan CM, Braffett BH, Gubitosi-Klug RA, Lorenzi GM, Luchsinger JA, Trapani VR, Bebu I, Chaytor N, Hitt SM, Farrell K, Lachin JM; DCCT/EDIC Research Group. Cognitive performance declines in older adults with type 1 diabetes: results from 32 years of follow-up in the DCCT and EDIC Study. *Lancet Diabetes Endocrinol*. 2021 Jul;9(7):436-445. doi: 10.1016/S2213-8587(21)00086-3. Epub 2021 May 27. PMID: 34051936; PMCID: PMC8583716.
- Reiss AL, Jo B, Arbelaez AM, Tsalikian E, Buckingham B, Weinzimer SA, Fox LA, Cato A, White NH, Tansey M, Aye T, Tamborlane W, Englert K, Lum J, Mazaika P, Foland-Ross L, Marzelli M, Mauras N; Diabetes Research in Children Network (DirecNet) Consortium. A Pilot randomized trial to examine effects of a hybrid closed-loop insulin delivery system on neurodevelopmental and cognitive outcomes in adolescents with type 1 diabetes. *Nat Commun*. 2022 Aug 30;13(1):4940. doi: 10.1038/s41467-022-32289-x. PMID: 36042217; PMCID: PMC9427757.
- 7. Jaser SS, Jordan LC. Brain Health in Children with Type 1 Diabetes: Risk and Protective Factors. Curr Diab Rep. 2021 Mar 14;21(4):12. doi: 10.1007/s11892-021-01380-w.
- 8. Musen G, Tinsley LJ, Marcinkowski KA, Pober D, Sun JK, Khatri M, Huynh R, Lu A, King GL, Keenan HA. Cognitive Function Deficits Associated With Long-Duration Type 1 Diabetes and Vascular Complications. *Diabetes Care*. 2018 Aug;41(8):1749-1756. doi: 10.2337/dc17-1955. Epub 2018 Jun 5. PMID: 29871904; PMCID: PMC6054500.
- 9. de Wit M, Gajewska KA, Goethals ER, McDarby V, Zhao X, Hapunda G, Delamater AM, DiMeglio LA. ISPAD Clinical Practice Consensus Guidelines 2022: Psychological care of children, adolescents and young adults with diabetes. *Pediatr Diabetes*. 2022 Dec;23(8):1373-1389. doi: 10.1111/pedi.13428. Epub 2022 Dec 5. PMID: 36464988



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#### **THANK YOU!**



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