Background Draft

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Prediabetes

Definitions: Type 2 Diabetes and Prediabetes

Diabetes mellitus is a disease where the body has abnormally elevated levels of blood glucose (hyperglycemia). Normally, the blood glucose level is reduced by the hormone insulin, which signals cells to absorb glucose from the blood. In type 1 diabetes, the beta cells that produce insulin are damaged, causing lower levels of insulin and higher levels of glucose. In **type 2 diabetes**, the elevated blood glucose levels are caused by *insulin resistance*: the glucose-absorbing cells are less sensitive to the insulin signal and thus absorb less glucose. ("Diabetes" n.d.; "Types of Diabetes :: Diabetes Education Online" n.d.; Colberg et al. 2016) This paper will focus on type 2 diabetes and the biological conditions that typically precede type 2 diabetes, which are discussed in the following paragraph.

Prediabetes refers to the state of hyperglycemia (high blood glucose levels) that is less severe than diabetes but has the potential to develop into type 2 diabetes. This intermediate state does not have a clear definition in existing literature, as seen in varying diagnosis criteria and biological phenotypes. Although large health organizations, such as American Diabetes Association (ADA), World Health Organization (WHO), and International Expert Committee (ICE), do not agree on the specific criteria for diagnosing prediabetes, they *do* generally agree that prediabetes can be identified through tests for *impaired fasting glycemia (IFG)*, *impaired glucose tolerance (IGT)*, and *glycated hemoglobin* (HbA_{1C}). IFG, IGT, and HbA_{1C} are also associated with increased risk of cardiovascular diseases. (Echouffo-Tcheugui, Kengne, and Ali 2018; Kleinherenbrink et al. 2018) The umbrella term for risk of developing diabetes and/or cardiovascular diseases is *cardiometabolic risk*, which is "a consequence of the presence of insulin resistance and atherogenic dyslipidemia." (Ruilope et al. 2007, 60).

Intervention

Type 2 diabetes interventions include lifestyle changes (Glechner et al. 2018) (dietary modifications (Guess 2018) and/or physical activity), drug treatments (Moin et al. 2018), and bariatric surgery (Ang 2018), with "lifestyle modification appearing to be the best therapeutic approach to prediabetes globally" (Echouffo-Tcheugui, Kengne, and Ali 2018, 7). This paper will focus on examining the intervention effects of **physical activity**.

Physical Activity

Regular physical activity lowers the risk for many diseases, including cardiometabolic risk (Leavitt, n.d.; World Health Organization 2010).

Guidelines

The US government has issued "2008 Physical Activity Guidelines for Americans" (Leavitt, n.d.), which details the health benefits of physical activity and provides weekly guidelines for the type, duration and intensity of physical activity that different groups of people (children/adolescents, adults, older adults, pregnant women, adults with disabilities, people with chronic medical conditions) should engage in. For example, adults should focus on performing moderate to vigorous intensity aerobic activity (75min-300min per week, depending on intensity) and add muscle-strengthening activities on 2 or more days of the week for further health benefits.

On an international scale, The World Health Organization's (WHO) "global recommendations on physical activity for health" (World Health Organization 2010) provides very similar guidelines.

The American Diabetes Association (ADA) agree with the above guidelines but focuses more on physical activity recommendations for the specific case of *diabetes*. For example, individuals with type 2 diabetes benefit from *regular* (daily) activity that maintains the *transient* effect of exercise on insulin action. Furthermore, for managing blood glucose levels, "engaging in combined aerobic and resistance training appears to be superior to undertaking either type of training on its own" (Colberg 2017, 3). While the US government and WHO mainly focus on aerobic and resistance/muscle-strengthening activities, the ADA also suggests that flexibility and balance exercises, such as yoga, can benefit blood glucose level management as well as general joint mobility, which is restricted as a result of hyperglycemia and aging. The ADA supplements these recommendations with associated diabetic health concerns. For example, very intense exercise can boost blood glucose levels, and individuals with diabetes-related vascular health complications should take precautions before engaging in physical activity. However, while acknowledging these health concerns, ADA's overall stance is that "pre-exercise medical clearance is not necessary for asymptomatic, sedentary individuals who wish to begin low- or moderate-intensity physical activity not exceeding the demands of brisk walking or everyday living" (unlike American College of Sports Medicine (ACSM), which recommends medical clearance) (Colberg 2017; Colberg et al. 2016).

Physical Activity as an Intervention for Type 2 Diabetes

Overall, lifestyle changes are an effective intervention for type 2 diabetes, as shown in 16 randomized controlled trials with intervention follow-ups ranging from one to six years (Glechner et al. 2018). The effectiveness is determined by a low (< 1) *relative risk* for type 2 diabetes, which is calculated by

$$\frac{\text{percentage of participants with diabetes in intervention group}}{\text{percentage of participants with diabetes in control group}}$$

Among these studies, (Pan et al. 1997) (6 year follow-up) is an example that physical activity, standalone or combined with dieting, significantly decreases risk for type 2 diabetes, as measured mainly by incidence of diabetes per 100 person-years. This study also reports changes in measures of blood glucose levels and weight.

Strong-D Study

Stanford's Strong-D study aims to evaluate different types of exercise regimens (strength, aerobic and a combination of both) as an intervention for normal weight type 2 diabetes ("STRONG-d. DISCOVeR Lab: Research" n.d.). This study has two interesting aspects:

1. Comparison of strength versus aerobic exercise regimens
2. Use of smartwatch/biosensor technology

TODO: Strength/Resistance exercise

Possible advantages:

- Distinction between different types of exercises, rather than generalizing that exercise is an effective intervention
- Depending on the participants' profiles and the results of each type of exercise regimen, can personalize exercise regimen recommendation based on the participant's profile
  - vs recommending the exercise regimen that is *overall* most effective for reducing risk of diabetes

TODO: (Ashton et al. 2018)

TODO: Use of technology in exercise interventions for type 2 diabetes

Possible advantages:

- detailed biosensor data
- personalization
- other advantages, e.g.:
  - Yates et al. investigated the effectiveness of educating IGT (impaired fasting glycemia) individuals about implementing walking as an IGT intervention. One group received an education program that focused on strategies that incorporated pedometers, while another group received a standard education program that focused on time-based strategies. Compared to a control group, the pedometer group showed significant decrease in blood glucose levels, while the standard education group did not show any significant improvements. (Yates et al. 2009; Glechner et al. 2018)

References

Ang, Gary Yee. 2018. "Reversibility of Diabetes Mellitus: Narrative Review of the Evidence." *World Journal of Diabetes* 9 (7): 127–31. https://doi.org/10.4239/wjd.v9.i7.127.

Ashton, Ruth E., Garry A. Tew, Jonathan J. Aning, Stephen E. Gilbert, Liane Lewis, and John M. Saxton. 2018. "Effects of Short-Term, Medium-Term and Long-Term Resistance Exercise Training on Cardiometabolic Health Outcomes in Adults: Systematic Review with Meta-Analysis." *Br J Sports Med*, June, bjsports–2017–098970. https://doi.org/10.1136/bjsports-2017-098970.

Colberg, Sheri R. 2017. "Key Points from the Updated Guidelines on Exercise and Diabetes." *Frontiers in Endocrinology* 8 (February). https://doi.org/10.3389/fendo.2017.00033.

Colberg, Sheri R., Ronald J. Sigal, Jane E. Yardley, Michael C. Riddell, David W. Dunstan, Paddy C. Dempsey, Edward S. Horton, Kristin Castorino, and Deborah F. Tate. 2016. "Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association." *Diabetes Care* 39 (11): 2065–79. https://doi.org/10.2337/dc16-1728.

"Diabetes." n.d. Text. Accessed October 3, 2018. https://medlineplus.gov/diabetes.html.

Echouffo-Tcheugui, Justin B., Andre P. Kengne, and Mohammed K. Ali. 2018. "Issues in Defining the Burden of Prediabetes Globally." *Current Diabetes Reports* 18 (11): 105. https://doi.org/10.1007/s11892-018-1089-y.

Glechner, Anna, Lina Keuchel, Lisa Affengruber, Viktoria Titscher, Isolde Sommer, Nina Matyas, Gernot Wagner, Christina Kien, Irma Klerings, and Gerald Gartlehner. 2018. "Effects of Lifestyle Changes on Adults with Prediabetes: A Systematic Review and Meta-Analysis." *Primary Care Diabetes* 12 (5): 393–408. https://doi.org/10.1016/j.pcd.2018.07.003.

Guess, Nicola D. 2018. "Dietary Interventions for the Prevention of Type 2 Diabetes in High-Risk Groups: Current State of Evidence and Future Research Needs." *Nutrients* 10 (9). https://doi.org/10.3390/nu10091245.

Kleinherenbrink, W., E. Osei, H. M. den Hertog, and A. a. M. Zandbergen. 2018. "Prediabetes and Macrovascular Disease: Review of the Association, Influence on Outcome and Effect of Treatment." *European Journal of Internal Medicine* 55: 6–11. https://doi.org/10.1016/j.ejim.2018.07.001.

Leavitt, Michael O. n.d. "2008 Physical Activity Guidelines for Americans," 76.

Moin, Tannaz, Julie A. Schmittdiel, James H. Flory, Jessica Yeh, Andrew J. Karter, Lydia E. Kruge, Dean Schillinger, Carol M. Mangione, William H. Herman, and Elizabeth A. Walker. 2018. "Review of Metformin Use for Type 2 Diabetes Prevention." *American Journal of Preventive Medicine*, August. https://doi.org/10.1016/j.amepre.2018.04.038.

Pan, X.-R., G.-W. Li, Y.-H. Hu, J.-X. Wang, W.-Y. Yang, Z.-X. An, Z.-X. Hu, et al. 1997. "Effects of Diet and Exercise in Preventing NIDDM in People with Impaired Glucose Tolerance: The Da Qing IGT and Diabetes Study." *Diabetes Care* 20 (4): 537–44. https://doi.org/10.2337/diacare.20.4.537.

Ruilope, Luis M, Hypertension Unit, 12 de Octubre Hospital, Madrid, Alejandro de la Sierra, Hypertension Unit, Hospital Clinic, Barcelona, Julian Segura, Hypertension Unit, 12 de Octubre Hospital, Madrid, Jose A Garcia-Donaire, and Hypertension Unit, 12 de Octubre Hospital, Madrid. 2007. "The Meaning of Cardiometabolic Risk in Hypertensive Patients." *US Endocrinology* 00 (1): 60. https://doi.org/10.17925/USE.2007.00.1.60.

"STRONG-d. DISCOVeR Lab: Research." n.d. Accessed October 6, 2018. http://med.stanford.edu/discover/research/strong-d.html.

"Types of Diabetes :: Diabetes Education Online." n.d. Accessed October 3, 2018. https://dtc.ucsf.edu/types-of-diabetes/.

World Health Organization. 2010. *Global Recommendations on Physical Activity for Health.* Geneva: World Health Organization.

Yates, Thomas, Melanie Davies, Trish Gorely, Fiona Bull, and Kamlesh Khunti. 2009. "Effectiveness of a Pragmatic Education Program Designed to Promote Walking Activity in Individuals with Impaired Glucose Tolerance: A Randomized Controlled Trial." *Diabetes Care* 32 (8): 1404–10. https://doi.org/10.2337/dc09-0130.