

## **Spousal diabetes – protocol development**

### ***Prevention of type 2 diabetes***

Approximately 90-95% of all diabetes cases are type 2 diabetes (T2D)<sup>(1)</sup>. Although genetic factors are strong predictors for the development of T2D<sup>(2)</sup>, and being genetically related to a person with T2D increases the relative risk of T2D by up to more than 30 times depending on number and type of probands<sup>(3)</sup>, most of the variation in the risk of T2D is explained by lifestyle and behavioural factors, or by the interaction of lifestyle behaviours with genetic factors<sup>(4-6)</sup>. Evidence regarding prevention or postponement of the onset of T2D in high risk individuals through a healthy diet, increased physical activity, and weight loss has been successfully established in randomized clinical trials from both high-income<sup>(7,8)</sup> and middle-income countries<sup>(9,10)</sup>. However, it remains unclear how the evidence from the available efficacy trials can be translated into low-cost, effective, feasible and sustainable interventions<sup>(17)</sup>, and how to efficiently identify high risk individuals as the target of the interventions.

### ***Early detection of type 2 diabetes***

Early detection of T2D is key for the management of the disease as diabetes related complications like retinopathy and cardio-vascular diseases can be prevented by controlling blood glucose levels and managing vascular risk factors<sup>(18,19)</sup>. However, globally 46% of people with diabetes are unaware of their disease status and thus receive no treatment<sup>(20)</sup>. The high proportion of undetected or late detected diabetes in high-income countries may be due to the current T2D screening recommendations, which focus on demographic (e.g., age, ethnicity), behavioural risk factors (e.g., overweight, physical inactivity), and first degree relatives with T2D<sup>(21)</sup>. In many low-income countries screening programs do not even exist, and due to limited diagnostic equipment<sup>(22-24)</sup>, and low awareness both in the population<sup>(25,26)</sup> and among the health professionals<sup>(24)</sup>, screening strategies from high-income countries cannot easily be adapted.

### ***Focusing on the family***

Results of studies<sup>(27-29)</sup> suggest that unhealthy eating patterns, physical inactivity, and obesity cluster among individuals living in the same household. In addition, married couples have been found to have similar weight measurements, and diet and physical activity behaviours<sup>(30)</sup>, which may explain why spouses of a person with T2D have an up to 30% higher risk of developing diabetes as compared to individuals with no spousal diabetes history<sup>(3,31)</sup>. Conversely, shared environment may also be a driver for positive influences. In a recently published study<sup>(32)</sup>, we showed that sharing a household with a

person who had been diagnosed with T2D for at least two years and who had received diabetes-related education was associated with an improved cardio-metabolic risk profile compared to individuals living in household without a member with diagnosed diabetes. These results are supported by studies from the U.S. showing that untreated spouses experienced weight loss<sup>(33,34)</sup> and improved their diet<sup>(35)</sup> when sharing a household with a spouse enrolled in a lifestyle intervention program. Thus, households present a challenge of socially entrenched unhealthy behaviours, but also a unique opportunity for identification of individuals at high risk of T2D and potentially detection of the disease.

#### Reference List

1. IDF. IDF Diabetes Atlas Sixth Edition. 2013. International Diabetes Federation.
2. Wilson PW, Meigs JB, Sullivan L, Fox CS, Nathan DM, D'Agostino RB, Sr.: Prediction of incident diabetes mellitus in middle-aged adults: the Framingham Offspring Study. *Arch Intern Med* 167:1068-1074, 2007
3. Hemminki K, Li X, Sundquist K, Sundquist J: Familial risks for type 2 diabetes in Sweden. *Diabetes Care* 33:293-297, 2010
4. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC: Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 345:790-797, 2001
5. Mozaffarian D, Kamineni A, Carnethon M, Djousse L, Mukamal KJ, Siscovick D: Lifestyle risk factors and new-onset diabetes mellitus in older adults: the cardiovascular health study. *Arch Intern Med* 169:798-807, 2009
6. Uusitupa MI, Stancakova A, Peltonen M, Eriksson JG, Lindstrom J, Aunola S, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Tuomilehto J, Laakso M: Impact of positive family history and genetic risk variants on the incidence of diabetes: the Finnish Diabetes Prevention Study. *Diabetes Care* 34:418-423, 2011
7. Knowler WC, Fowler SE, Hamman RF, Christophi CA, Hoffman HJ, Brenneman AT, Brown-Friday JO, Goldberg R, Venditti E, Nathan DM: 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet* 374:1677-1686, 2009
8. Lindstrom J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemio K, Hamalainen H, Harkonen P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Mannelin M, Paturi M, Sundvall J, Valle TT, Uusitupa M, Tuomilehto J: Sustained reduction in the incidence of type 2

diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet* 368:1673-1679, 2006

9. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP, Zheng H, Zhang H, Bennett PH, Howard BV: Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 20:537-544, 1997
10. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V: The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 49:289-297, 2006
11. Cooper RS, Rotimi CN, Kaufman JS, Owoaje EE, Fraser H, Forrester T, Wilks R, Riste LK, Cruickshank JK: Prevalence of NIDDM among populations of the African diaspora. *Diabetes Care* 20:343-348, 1997
12. Nielsen J, Christensen DL: Glucose intolerance in the West African Diaspora: a skeletal muscle fibre type distribution hypothesis. *Acta Physiol (Oxf)* 202:605-616, 2011
13. HALES CN, Barker DJ: Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 35:595-601, 1992
14. Kibirige D, Ssekitoleko R, Mutebi E, Worodria W: Overt diabetes mellitus among newly diagnosed Ugandan tuberculosis patients: a cross sectional study. *BMC Infect Dis* 13:122, 2013
15. Mugusi F, Swai AB, Alberti KG, McLarty DG: Increased prevalence of diabetes mellitus in patients with pulmonary tuberculosis in Tanzania. *Tubercle* 71:271-276, 1990
16. Ali MK, Magee MJ, Dave JA, Ofotokun I, Tungsiripat M, Jones TK, Levitt NS, Rimland D, Armstrong WS: HIV and Metabolic, Body, and Bone Disorders: What We Know From Low- and Middle-Income Countries. *J Acquir Immune Defic Syndr* 67 Suppl 1:S27-S39, 2014
17. Narayan KM, Gregg EW, Engelgau MM, Moore B, Thompson TJ, Williamson DF, Vinicor F: Translation research for chronic disease: the case of diabetes. *Diabetes Care* 23:1794-1798, 2000
18. Holman RR, Paul SK, Bethel MA, Neil HA, Matthews DR: Long-term follow-up after tight control of blood pressure in type 2 diabetes. *N Engl J Med* 359:1565-1576, 2008
19. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA: 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 359:1577-1589, 2008
20. Beagley J, Guariguata L, Weil C, Motala AA: Global estimates of undiagnosed diabetes in adults. *Diabetes Res Clin Pract* 103:150-160, 2014
21. Drivsholm, T. Hansen C., Kristensen, J. K., Lassen, B., and Schultz-Larsen, P. Type 2 diabetes - et metabolisk syndrom. 2012. Dansk Selskab for Almen Medicin (DSAM).

22. Baumann LC, Opio CK, Otim M, Olson L, Ellison S: Self-care beliefs and behaviors in Ugandan adults with type 2 diabetes. *Diabetes Educ* 36:293-300, 2010
23. Hjelm K, Atwine F: Health-care seeking behaviour among persons with diabetes in Uganda: an interview study. *BMC Int Health Hum Rights* 11:11, 2011
24. Peck R, Mghamba J, Vanobberghen F, Kavishe B, Rugarabamu V, Smeeth L, Hayes R, Grosskurth H, Kapiga S: Preparedness of Tanzanian health facilities for outpatient primary care of hypertension and diabetes: a cross-sectional survey. *Lancet Glob Health* 2:e285-e292, 2014
25. Awah PK, Unwin N, Phillimore P: Cure or control: complying with biomedical regime of diabetes in Cameroon. *BMC Health Serv Res* 8:43, 2008
26. Rutebemberwa E, Katureebe SK, Gitta SN, Mwaka AD, Atuyambe L: Perceptions of diabetes in rural areas of Eastern Uganda. *Curationis* 36:E1-E7, 2013
27. Christakis NA, Fowler JH: The spread of obesity in a large social network over 32 years. *N Engl J Med* 357:370-379, 2007
28. Pachucki MA, Jacques PF, Christakis NA: Social network concordance in food choice among spouses, friends, and siblings. *Am J Public Health* 101:2170-2177, 2011
29. Sonnevile KR, Rifas-Shiman SL, Kleinman KP, Gortmaker SL, Gillman MW, Taveras EM: Associations of obesogenic behaviors in mothers and obese children participating in a randomized trial. *Obesity (Silver Spring)* 20:1449-1454, 2012
30. Meyler D, Stimpson JP, Peek MK: Health concordance within couples: a systematic review. *Soc Sci Med* 64:2297-2310, 2007
31. Leong A, Rahme E, Dasgupta K: Spousal diabetes as a diabetes risk factor: A systematic review and meta-analysis. *BMC Med* 12:12, 2014
32. Nielsen J, Bahendeka SK, Gregg EW, Whyte SR, Bygbjerg IC, Meyrowitsch DW: A comparison of cardiometabolic risk factors in households in rural Uganda with and without a resident with type 2 diabetes, 2012-2013. *Prev Chronic Dis* 12:E44, 2015
33. Gorin AA, Wing RR, Fava JL, Jakicic JM, Jeffery R, West DS, Brelje K, Dilillo VG: Weight loss treatment influences untreated spouses and the home environment: evidence of a ripple effect. *Int J Obes (Lond)* 32:1678-1684, 2008
34. White E, Hurlich M, Thompson RS, Woods MN, Henderson MM, Urban N, Kristal A: Dietary changes among husbands of participants in a low-fat dietary intervention. *Am J Prev Med* 7:319-325, 1991
35. Shattuck AL, White E, Kristal AR: How women's adopted low-fat diets affect their husbands. *Am J Public Health* 82:1244-1250, 1992

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