Improved lifestyle and decreased diabetes risk over 13 years: The Finnish Experience

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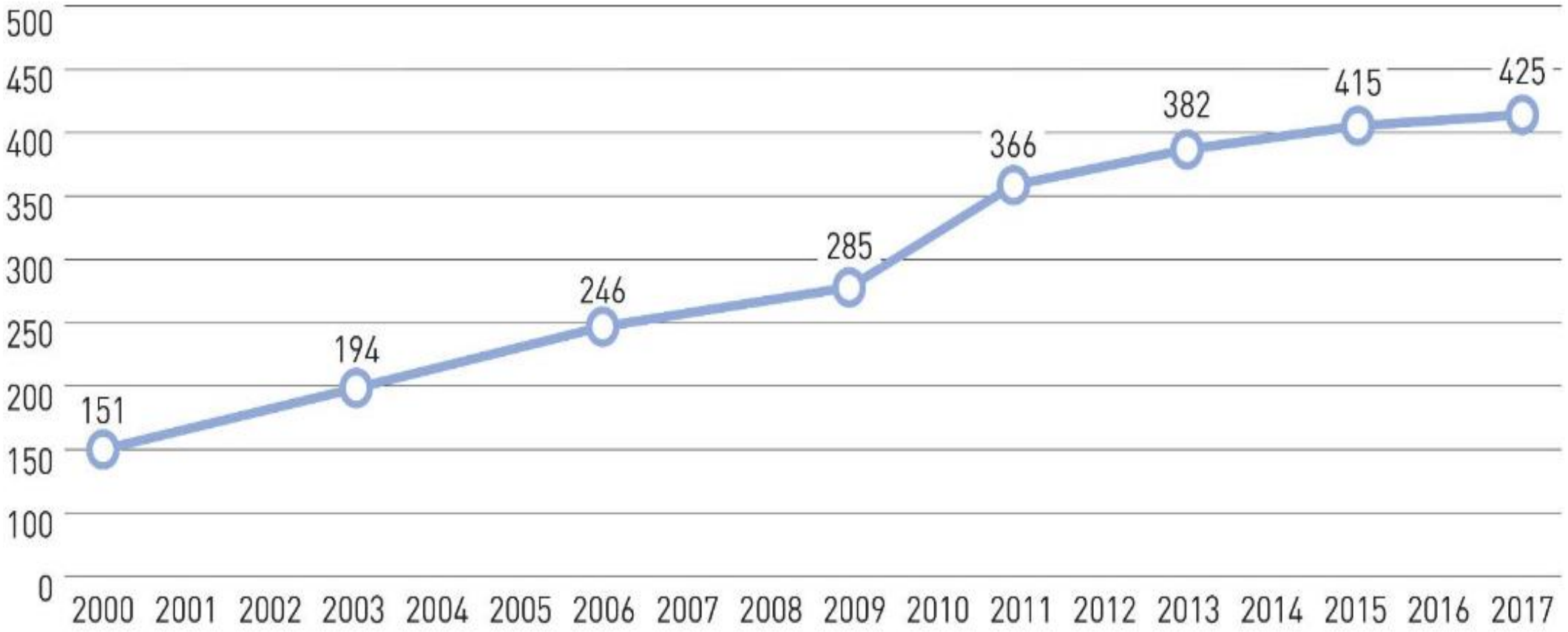
Content of the presentation

- Main risk factors of Type 2 diabetes (T2DM)
- Summary results from the Finnish Diabetes Prevention Study (DPS)
- Impact of genes, family history vs. lifestyles
- Post intervention results
- Practical implementations for prevention based on the Finnish experience
- Conclusions

Diabetes around the world

The number of adults (20-79 years) with diabetes has tripled during the last 2 decades, millions



IDF: Diabetes Atlas 2017

Type 2 diabetes risk factors

Risk markers

- Age
- Family history
- Gestational diabetes
- Delivery of macrosomic baby
- Ethnicity
- Low SES
- Low birth weight
- Metabolic syndrome
- Previous CVD
- Polycystic ovary syndrome, PCOS
- Non-alcoholic fatty liver disease, NAFLD
- Genetic markers

Modifiable risk factors

- Overweight / obesity
- Abdominal obesity
- Low physical activity
- Smoking
- Unhealthy diet

Possibly modifiable risk factors

- Sleep deprivation
- Distress and depression
- Persistent organic pollutants (e.g. pesticides, solvents, pharmaceuticals)
- Microbiota

Prevention of type 2 diabetes by lifestyle intervention – the evidence

Study	Intervention	N	Drop-out rate	FU time	Risk reduction	Ref
The Da-Qing Study **China**	**Diet** **Exercise** **Diet+exercise** **Control**	**130** **141** **126** **133**	**8%**	**6 years**	**31%** **46%** **42%**	Pan et al. 1997. Diabetes Care 20:537-544
The DPS **Finland**	**Diet+physical activity** **Control**	**265** **257**	**8%**	**3,2 years**	**58%**	Tuomilehto et al 2001. new Engl J Med
The DPP **USA**	**Diet+physical activity** **Metformin** **Placebo**	**1079** **1073** **1082**	**8%**	**2,8 years**	**58%** **31%**	DPP research group 2002. New Engl J Med 346:393-403
IDDP **India**	**Lifestyle** **Metformin** **Lifestyle+metformin** **Control**	**133** **133** **129** **136**	**5%**	**30 months**	**28,5%** **26,4%** **28,2%**	Ramachandran et al. 2006. Diabetologia 49:289-97
Japanese trial on IGT males **Japan**	**Diet+exercise** **Control**	**102** **356**	**5%**	**4 years**	**67,4%**	Kosaka et al 2005. Diabetes Res Clin Pract 67:152-162
The SLIM Study **The Netherlands**	**Diet+physical activity** **Control**	**74** **73**	**8%**	**3 years**	**58%**	Roumen et al. 2008. Diabetic Medicine 25:597-605
EDIPS Newcastle **UK**	**Diet+physical activity** **Control**	**51** **51**	**19%**	**3,1 years**	**55%**	Penn et al 2009. BMC Public Health 9

Finnish Diabetes Prevention Study (DPS)

- The first randomised controlled study to show that Type 2 diabetes is preventable by changing lifestyles
- Started in 1993 in Helsinki and Kuopio, other centres Turku, Tampere and Oulu
- Highly quoted
- Over 80 reasearch papers published so far
- Partner in international GWAS and biomarker consortia

The New England
Journal of Medicine

VOLUME 344 MAY 3, 2001 NUMBER 18

PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

JAAKKO TUOMILEHTO, M.D., PH.D., JAANA LINDSTRÖM, M.S., JOHAN G. ERIKSSON, M.D., PH.D., TIMO T. VALLE, M.D., HELENA HÄMÄLÄINEN, M.D., PH.D., PIRJO ILANNE-PARIKKA, M.D., SIRKKA KEINÄNEN-KIUKAANNIEMI, M.D., PH.D., MAURI LAAKSO, M.D., ANNE LOUHERANTA, M.S., MERJA RASTAS, M.S., VIRPI SALMINEN, M.S., AND MATTI UUSITUPA, M.D., PH.D., FOR THE FINNISH DIABETES PREVENTION STUDY GROUP

Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study

Jaana Lindström, Pirjo Ilanne-Parikka, Markku Peltonen, Sirkka Aunola, Johan G Eriksson, Katri Hemiä, Helena Hämäläinen, Pirjo Härkönen, Sirkka Keinänen-Kiukaanniemi, Mauri Laakso, Anne Louheranta, Marjo Mannelin, Merja Paturi, Jouko Sundvall, Timo T Valle, Matti Uusitupa, Jaakko Tuomilehto, on behalf of the Finnish Diabetes Prevention Study Group

Lancet 2006; 368: 1673-79
See Comment page 1634

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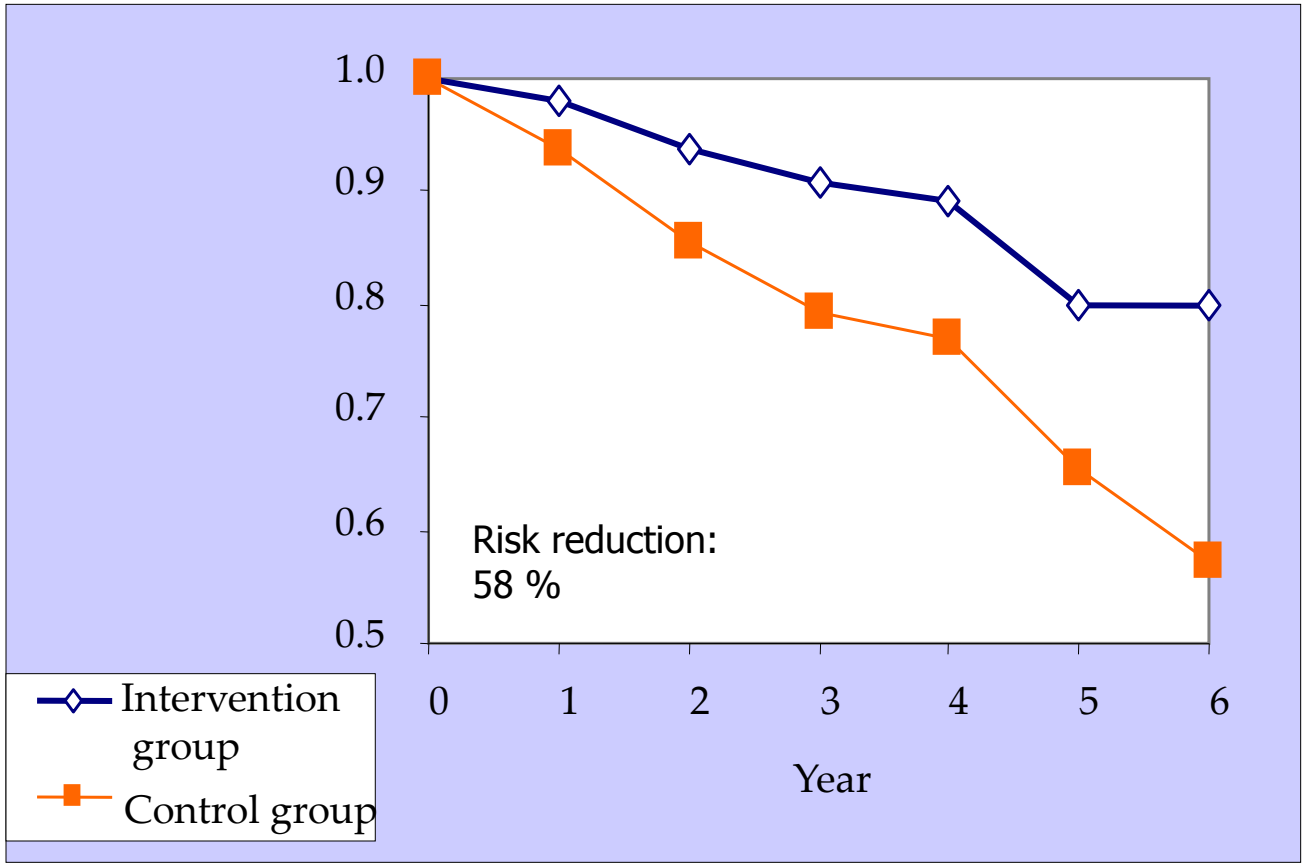
Summary

Background Lifestyle interventions can prevent the deterioration of impaired glucose tolerance to manifest type 2 diabetes, at least as long as the intervention continues. In the extended follow-up of the Finnish Diabetes Prevention Study, we assessed the extent to which the originally-achieved lifestyle changes and risk reduction remain after discontinuation of active counselling.

Development of diabetes during the lifestyle intervention in the intervention and control groups – DPS (Tuomilehto et al. NEJM 2001)

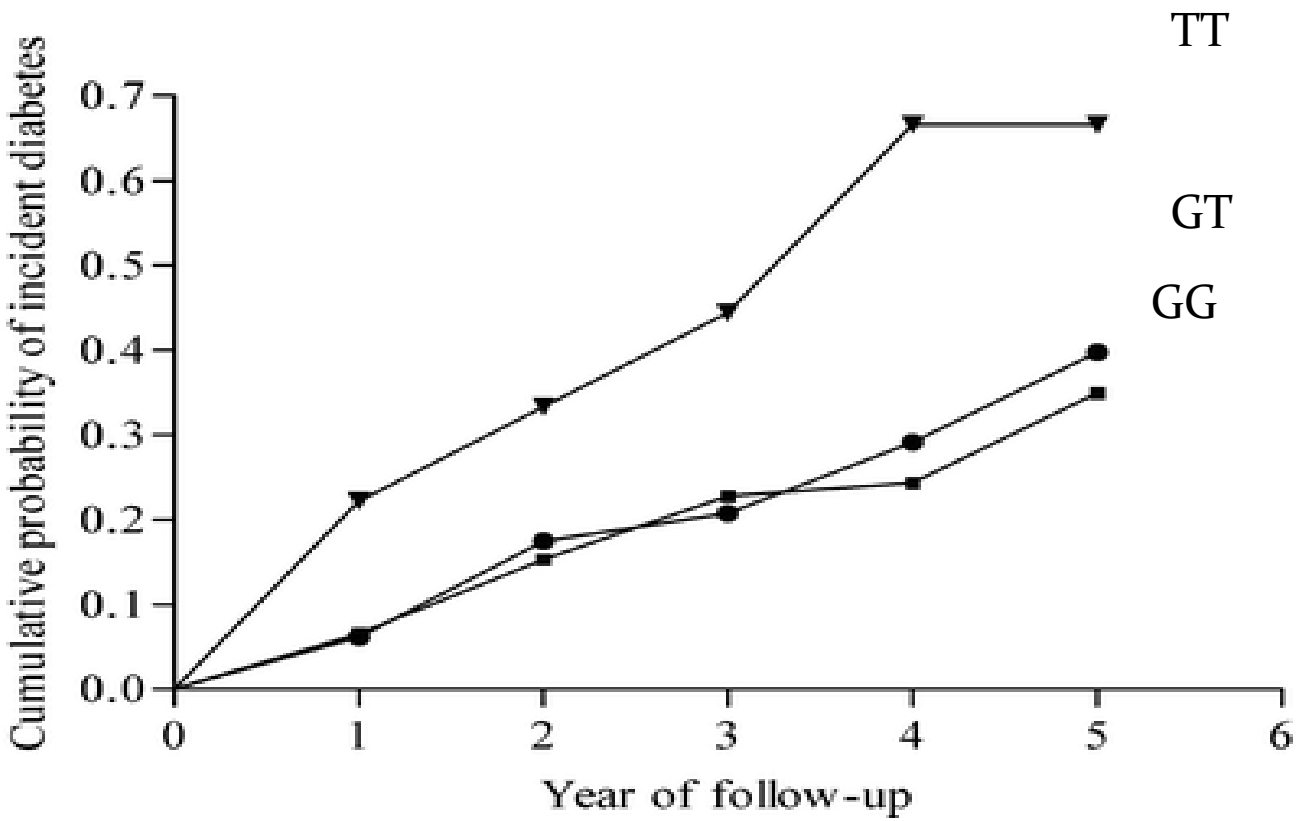


Genetics of Type 2 Diabetes

- Individual risk for T2DM is strongly influenced by genetic factors
- In aggregate, common genetic variants explain only a small fraction of disease
- No major role for low frequency variants, either (Locke A et al. Genetic architecture of Type 2 diabetes, Nature 2016)

- **Interaction studies in the DPS**: single gene polymorphisms and genetic risk score approach

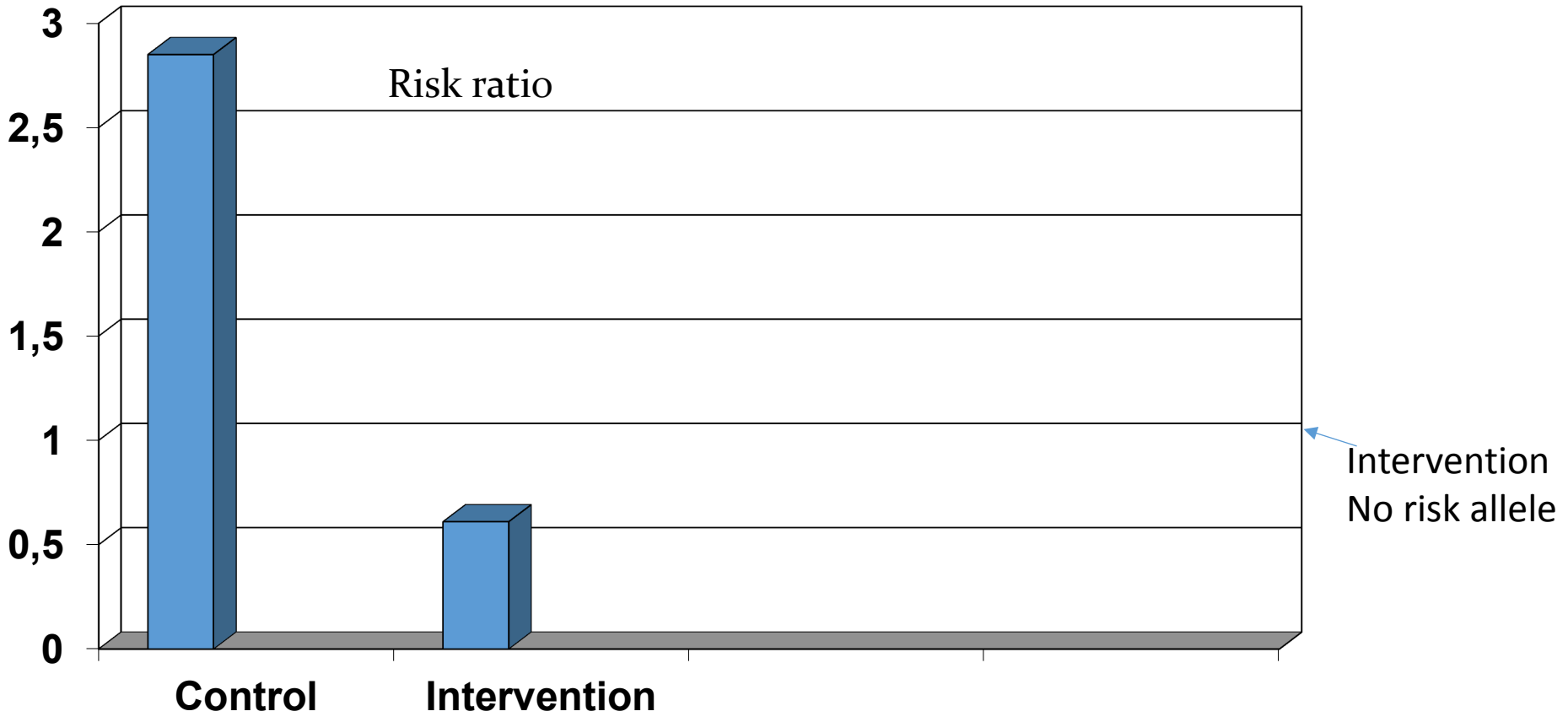
4-year probability of incident T2DM by *TCF7L2* rs 12255372 genotype – DPS control group



P=0.009

Wang et al. Diabetologia 2007

Gene-diet interaction with regard to *TCF7L2*-TT genotype of rs 12255372 - **DPS**



Wang et al. Diabetologia 2007

Pathophysiology/Complications
ORIGINAL ARTICLE

Impact of Positive Family History and Genetic Risk Variants on the Incidence of Diabetes

The Finnish Diabetes Prevention Study

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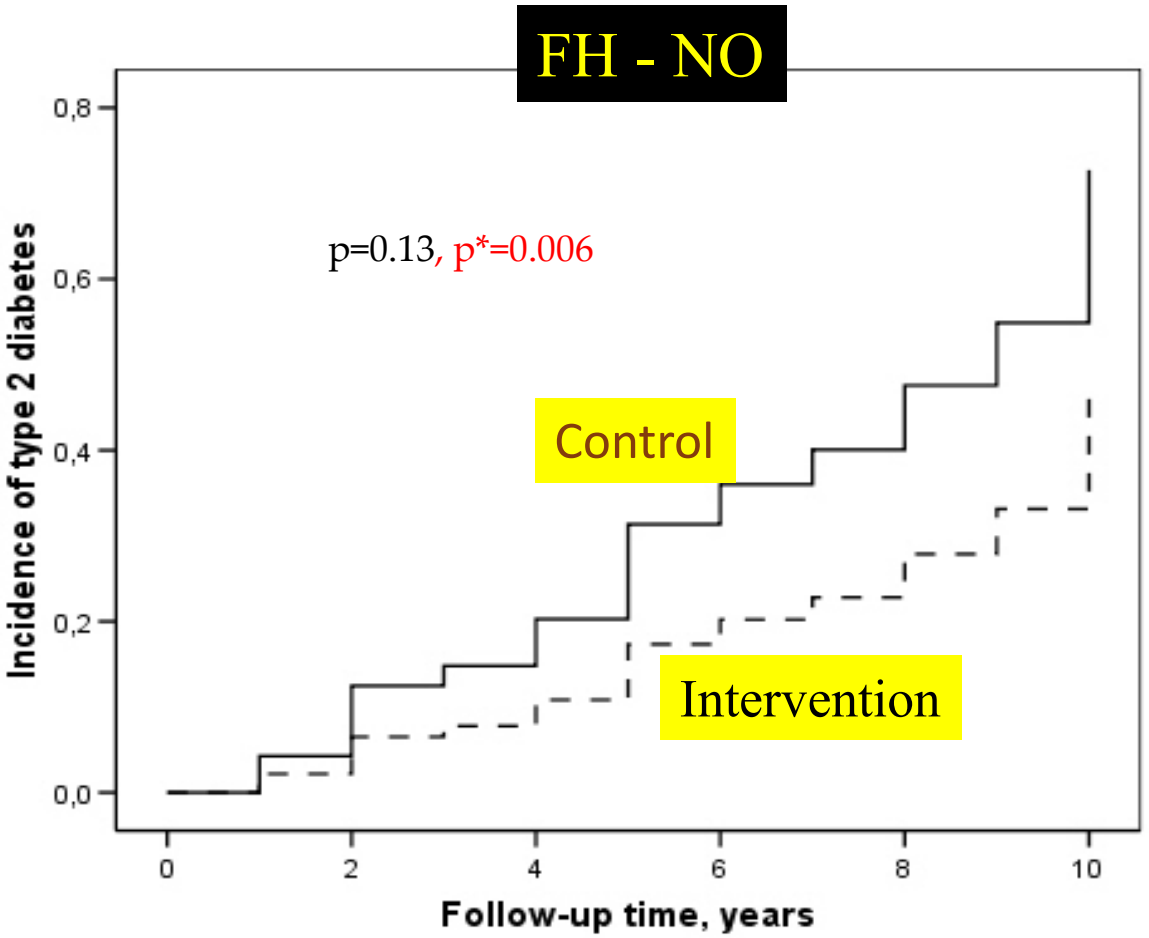
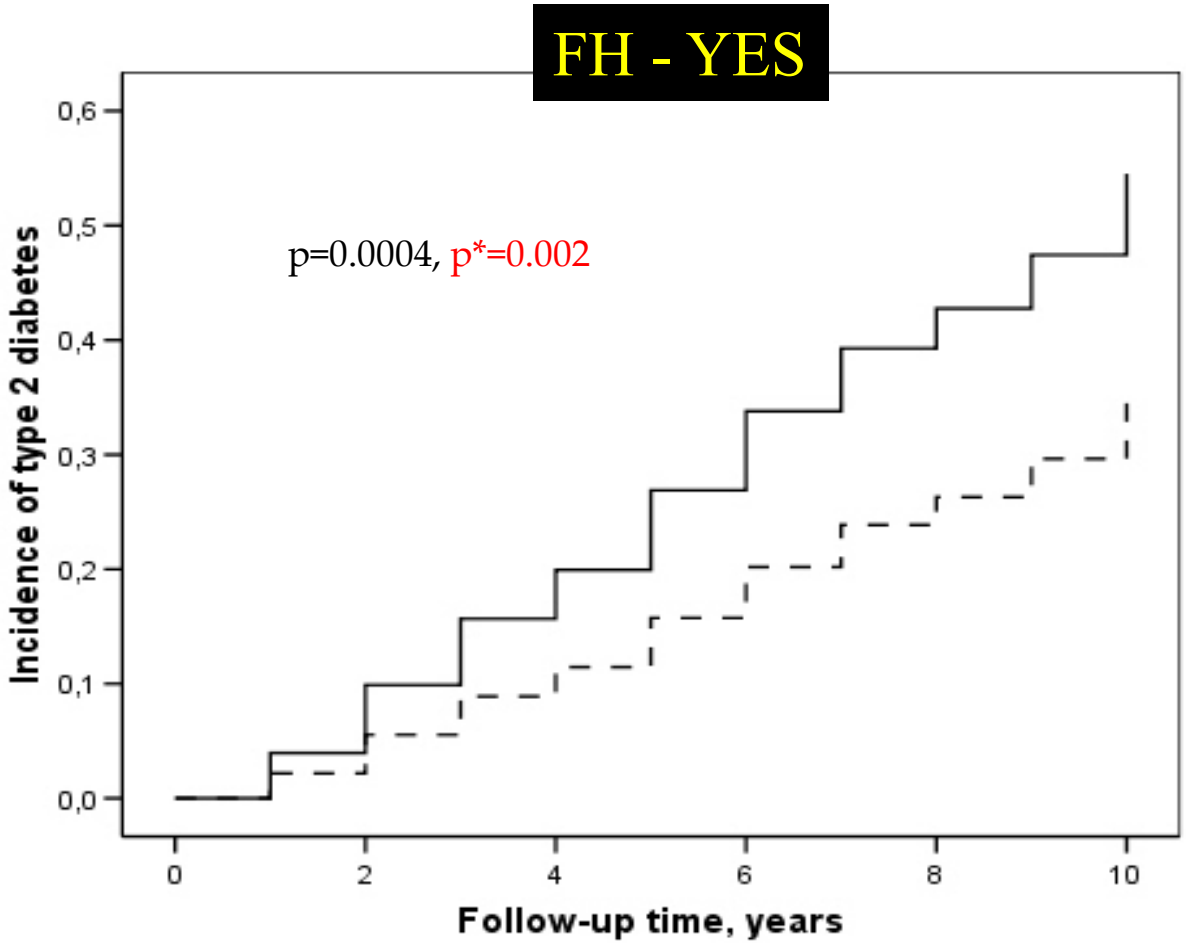
Both genetic and environmental factors play major roles in the development of type 2 diabetes mellitus. In recent years, the research aiming to explore the genetic basis of type 2 diabetes has progressed significantly. Currently, >30 genetic variants have been identified

Benefits of lifestyle prevention of diabetes according to the Family History (FH) of diabetes - DPS





Uusitupa, et al. Diabetes Care 2011

Genotyping

Nineteen type 2 diabetes-susceptibility SNPs (Taqman), 8 of them associated with insulin secretion

PPARG rs1801282, *KCNJ11* rs5219, *TCF7L2* rs7903146

SLC30A8 rs13266634, *HHEX* rs1111875, *CDKN2B* rs10811661

IGF2BP2 rs4402960, *CDKAL1* rs7754840, *FTO* rs9939609

HNF1B rs757210, *WFS1* rs10010131, *JAZF1* rs864745, *CDC123* rs12779790

TSPAN8 rs7961581, *THADA* rs7578597, *ADAMTS9* rs4607103

NOTCH2 rs10923931, *KCNQ1* rs2283228, *MTNR1B* rs10830963

Impact of FH and Genetic Risk Variants

A	HR	95% CI	p value
Family history of T2DM	0.78	(0.57; 1.06)	0.118
Genetic risk score (19 SNPs)	1.04	(0.90; 1.20)	0.617
Intervention vs. control group	0.55	(0.41; 0.75)	**1.2E-04**
B			
Family history of T2DM	0.80	(0.57; 1.11)	0.180
Genetic risk score (19 SNPs)	1.02	(0.87; 1.18)	0.840
Intervention vs. control group	0.52	(0.38; 0.72)	**5.9E-05**
Fasting glucose (baseline)	1.69	(1.44; 1.99)	**2.2E-10**
2-h glucose (baseline)	1.35	(1.14; 1.60)	**0.0005**
Fasting insulin (baseline)	1.25	(1.03; 1.53)	**0.025**
2-h insulin (baseline)	0.81	(0.63; 1.02)	0.076
BMI (baseline)	1.17	(0.98; 1.39)	0.077

Progressors vs non-progressors to T2D

	Progressors (143)	Non-progressors (312)	P*
BMI (kg/m^2)	31.9 ± 5.1	29.4 ± 4.2	<0.001
Δ BMI first year	-0.87 (-1.16; -0.57)	-1.21 (-1.39; -1.02)	0.04
Matsuda ISI†	3.16 (2.88; 3.44)	4.40 (4.19; 4.61)	<0.001
$AIGR_{0-30}$	31.0 (28.1; 33.8)	31.9 (30.0; 33.7)	0.26
ISI-adjusted $AIGR_{0-30}$†	22.0 (20.8; 23.2)	32.5 (31.4; 33.5)	<0.001

* For the effect of diabetes during the follow-up (progressor or non-progressor) after univariate ANOVA, GLM
adjusted for age, sex and study group. △BMI first year as BMI at year 1 - BMI at baseline
† Progressors, n=141 and non-progressors, n=310.

De Mello et al. Diabetes Care 2012

Diabetologia
DOI 10.1007/s00125-012-2752-5

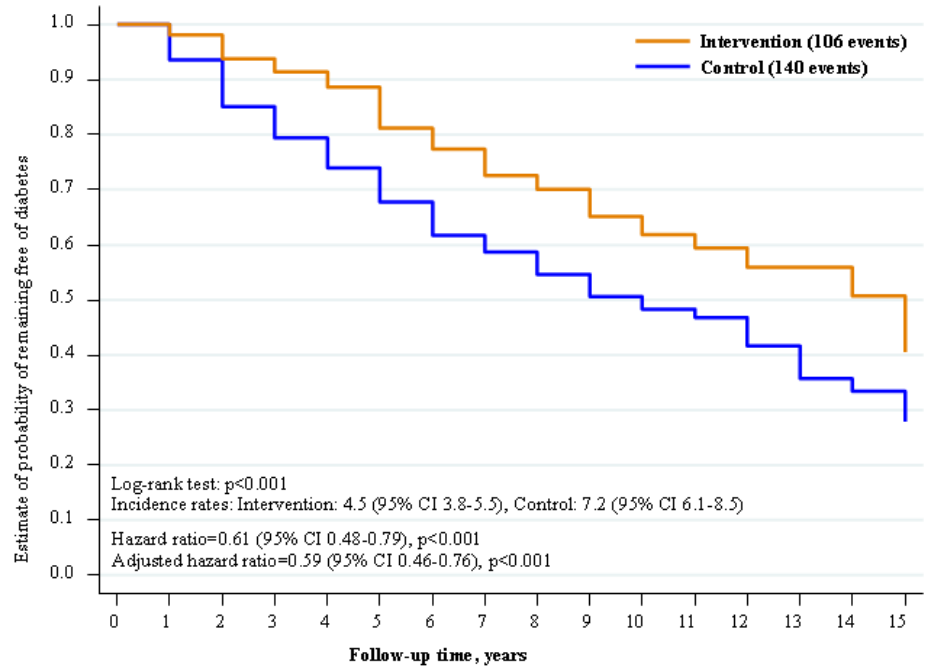
ARTICLE

Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS)

J. Lindström · M. Peltonen · J. G. Eriksson · P. Ilanne-Parikka · S. Aunola · S. Keinänen-Kiukaanniemi · M. Uusitupa · J. Tuomilehto · for the Finnish Diabetes Prevention Study (DPS)

Received: 31 May 2012 / Accepted: 7 September 2012

Incidence of Diabetes after 13 years of follow-up, Lindström J et al. Diabetologia 2013

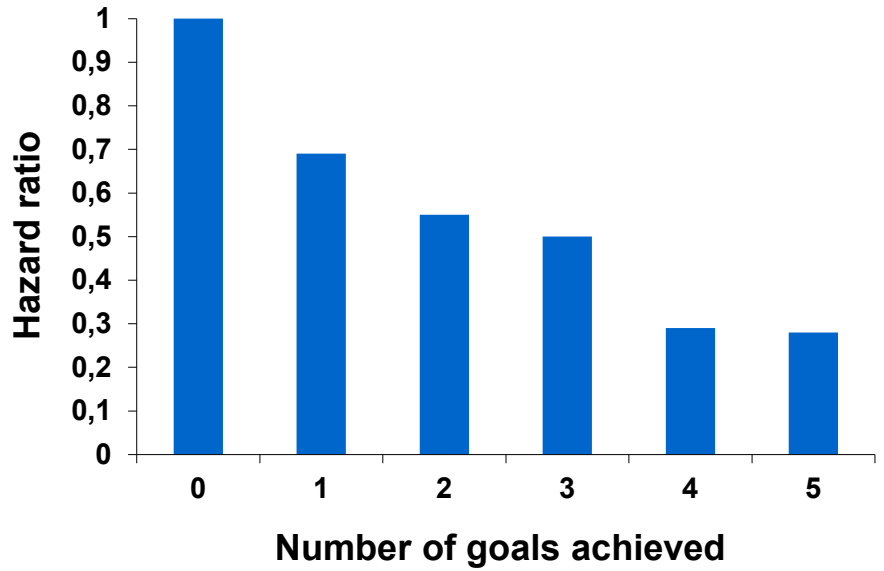


Number at risk

Intervention	261	238	193	158	83	10
Control	251	209	158	120	63	6

Adjusted HR: Adjusted for sex, age, 2h glucose and BMI at baseline.

The DPS: The more goals achieved, the lower the risk!

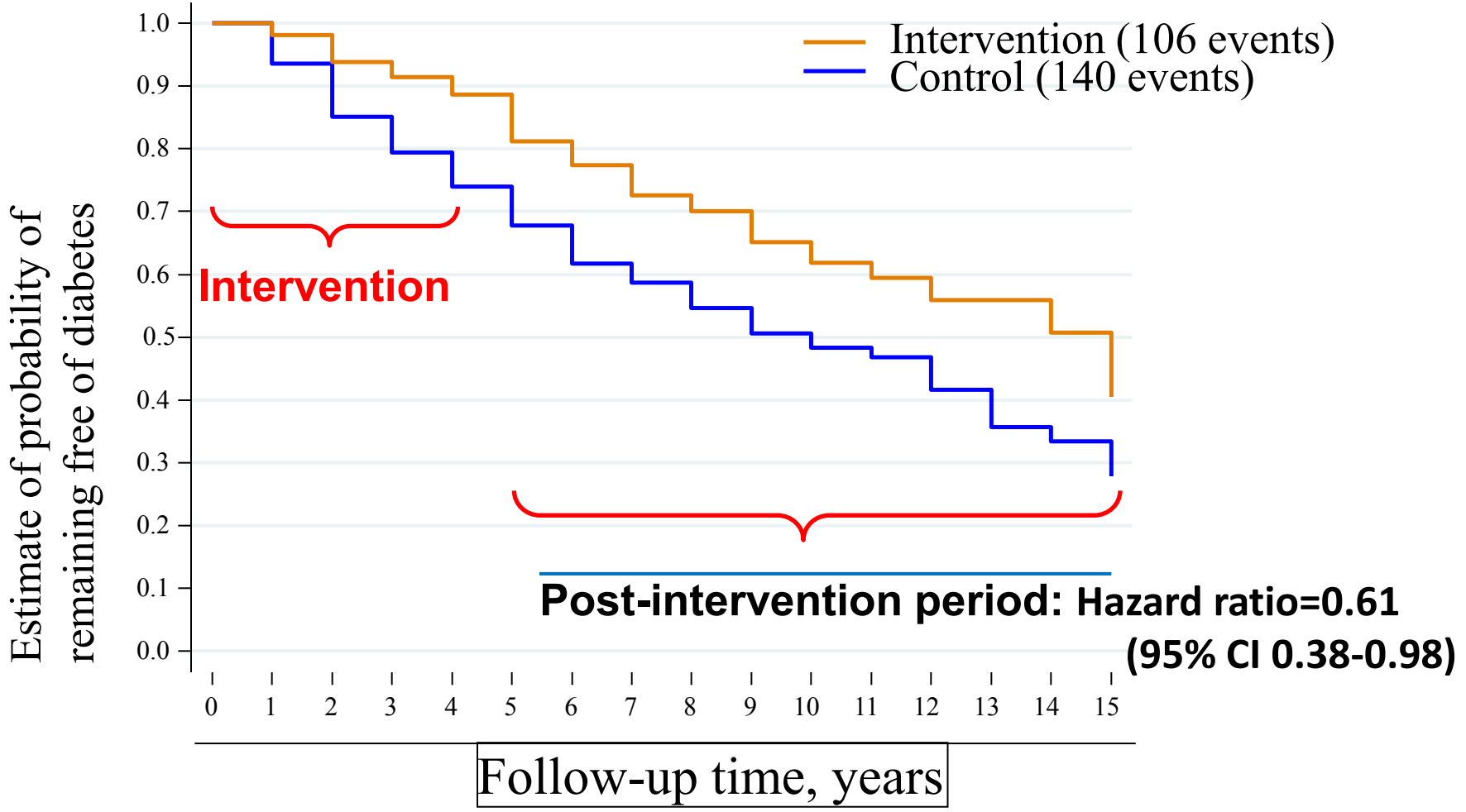


- Weight reduction ≥ 5%
- Moderate fat <30 E%
- Low saturated fat <10 E%
- High fibre ≥15g/1000kcal
- Physical activity ≥30 min /day

Goals at year 3; incidence during 13 years time-span
Adjusted for baseline age, bmi, 2h-glucose and sex

Lindström et al. Diabetologia. 2013.

The ABSOLUTE RISK DIFFERENCE in T2D incidence between groups did not diminish, but increased somewhat during the post-intervention follow-up period



Adjusted HR:
for sex, age, 2h glucose and BMI at baseline.

Lindström et al. Diabetologia. 2013

Development Programme for the Prevention and Care of Diabetes

DEHKO 2000–2010

Primary Prevention of Type 2 Diabetes

Programme for the Prevention of Type 2 Diabetes (2003–2010)
- Population Strategy
- High-Risk Strategy
- Strategy of Early Diagnosis and Management

Implementation of the Prevention Programme: FIN-D2D Project 2003–2007

Developing Diabetes Care and its Quality

Care Organization

Quality Criteria and Quality Monitoring Systems

Basic Education and Further Training of Health Care Staff

Modern Medication

Supporting Self-Care of Persons with Diabetes

Educatio

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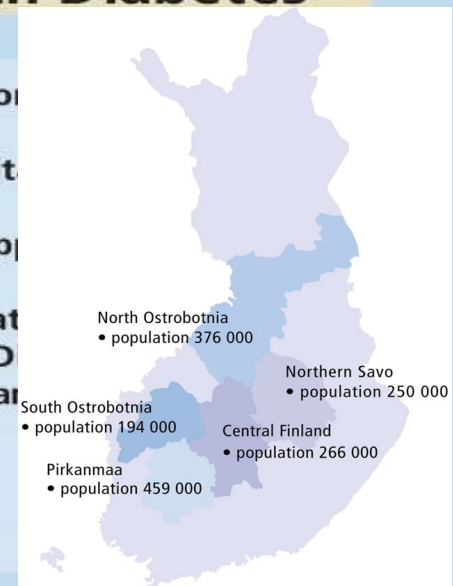
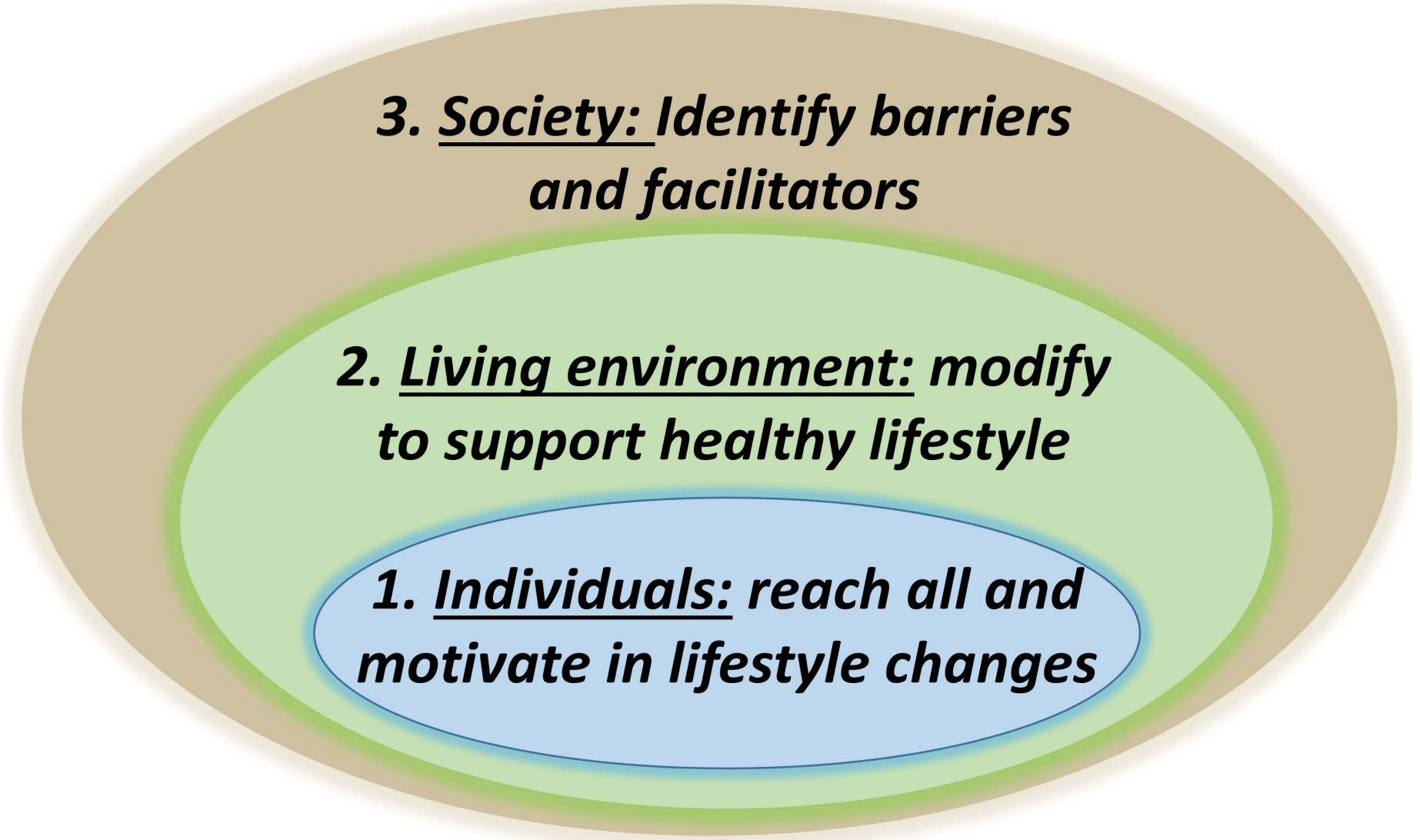


Influencing Municipal Decision-making

FIN-D2D: Positive experiences

- **Models of lifestyle intervention were proven feasible in primary health care**
- **Screening and risk assessment** became part of daily practice:
  - The FINDRISC; OGTT testing; waist circumference measurement
- **Treatment paths** were defined and health promotion units were established in all participating hospital districts
- **New ways of collaboration**
  - Multi-professional team work
  - Hospital districts, municipalities, health care centres, occupational health care, NGOs, pharmacies, research organizations
- **Nationwide recognition and increased awareness of obesity and diabetes problem**



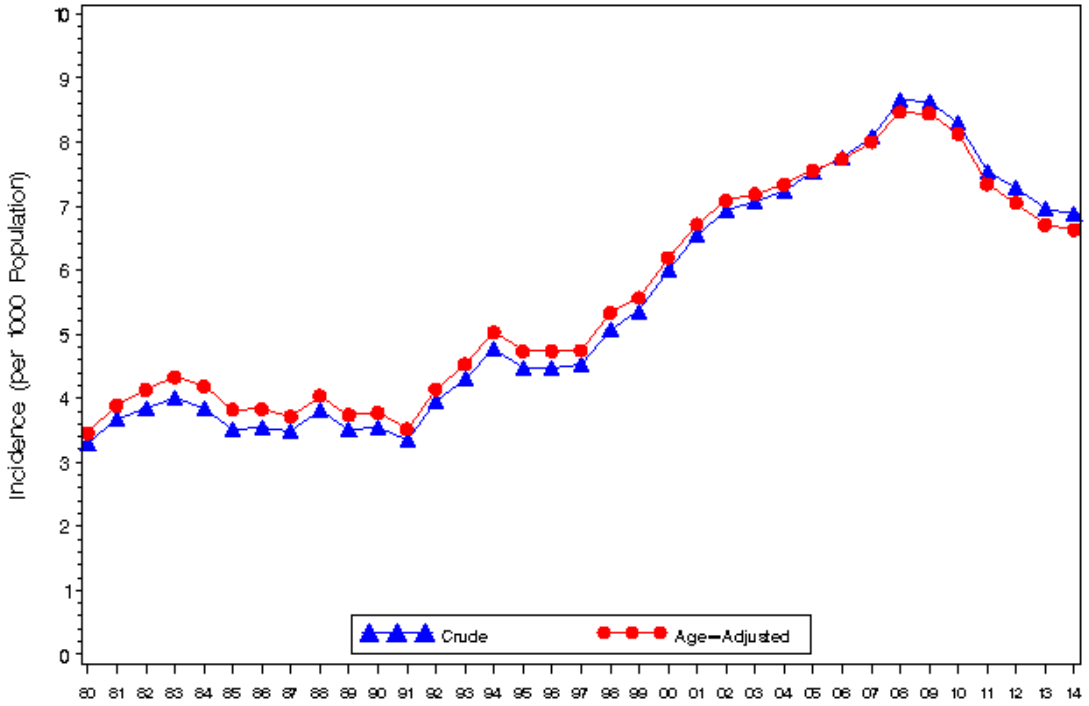
Central idea of StopDia project:
Three levels of action to stop diabetes

StopDia

Incidence of diagnosed diabetes

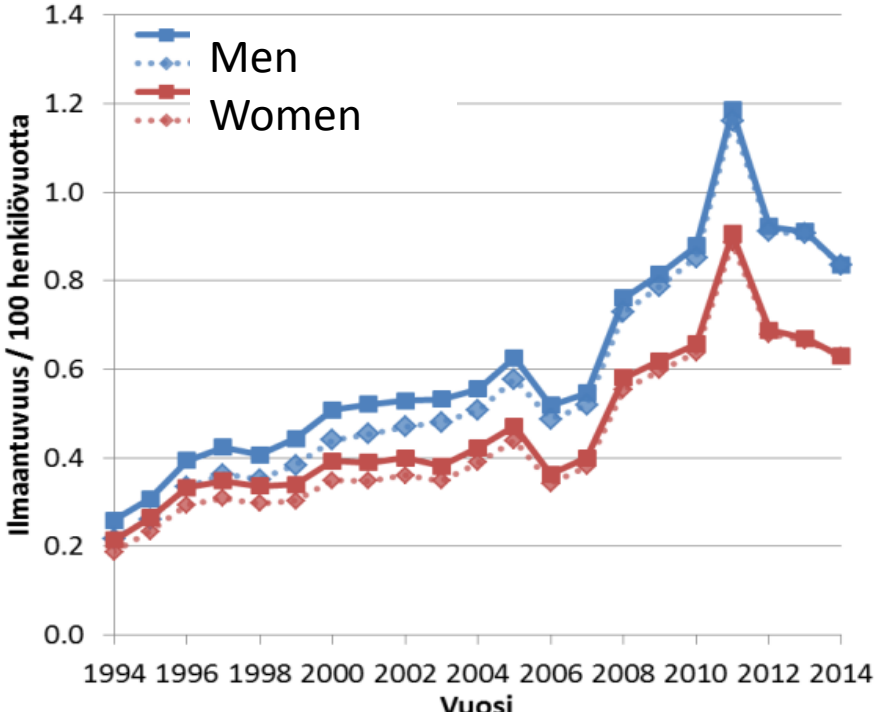
United States, 1980-2014:

http://www.cdc.gov/diabetes/statistics/incidence/fig2.htm

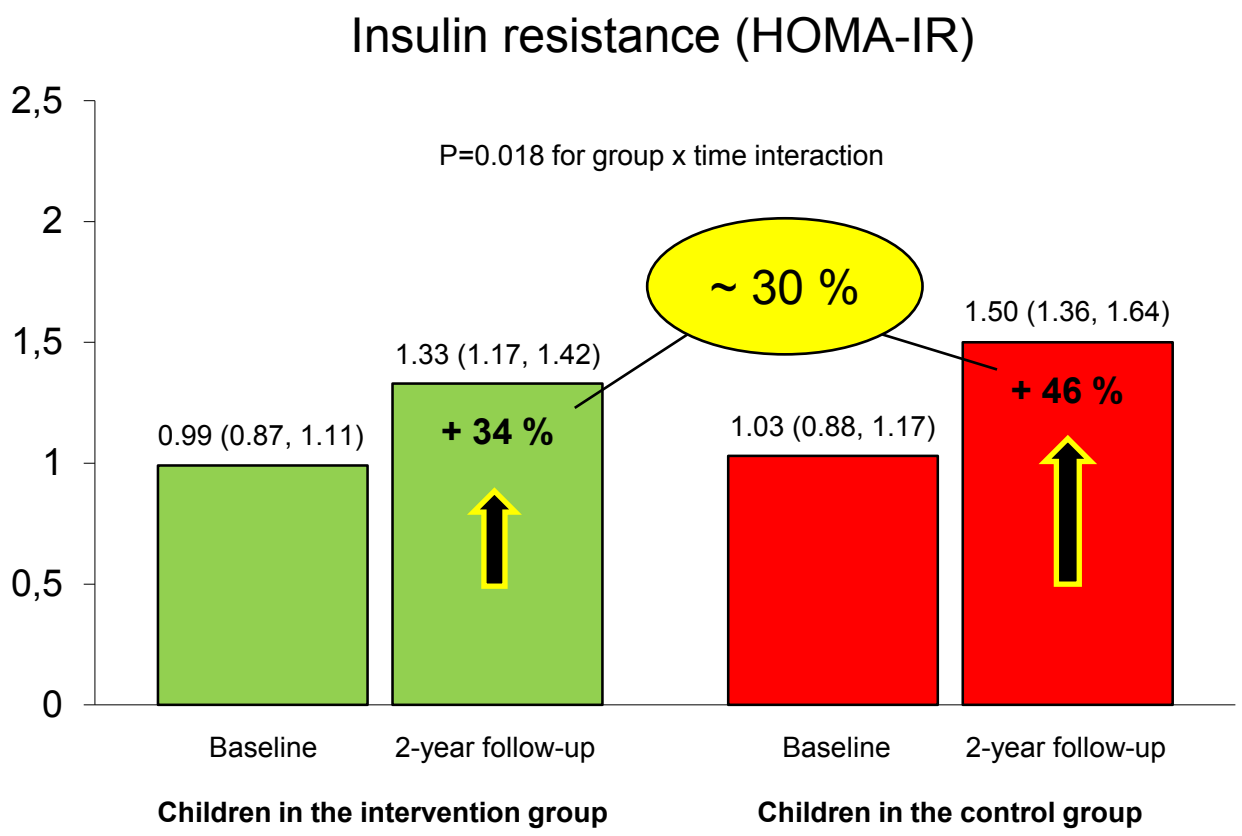


Finland, 1994-2014:

https://www.julkari.fi/handle/10024/125827



Two-year physical activity and dietary intervention effect on worsening insulin sensitivity in prepubertal and mainly normal weight children



Lakka TA et al. unpublished 2018

Practical implementations

Individual	Primary Health Care/District	Society
Awareness of the risk, screening (risk questionnaire)	Active screening of high risk individuals, gestational diabetes	County or national programmes to increase the awareness of T2DM
Positive family history, gestational diabetes	Training of health care staff (dietitians, nurses and physicians), motivation	Learning good practices from other stakeholders, investing in prevention facilities (including physical activity, healthy diet)
Permanent lifestyle changes, motivation	Increasing awareness of T2DM Investing into facilities	Taxation, food labeling, promoting physical activity in everyday life, healthy school lunches!

Conclusions

1. * We have unequivocal evidence that T2D is preventable by changing lifestyles, i.e. weight reduction, changing diet according to the current recommendations in terms of quality of fat, fiber intake (whole grain) and increased use of fruit and vegetables
2. * Risk reduction of T2D is strongly related to the degree of long-term weight loss and adherence to lifestyle changes, and the preventive effect has been demonstrated to sustain for many years after the active intervention
3. *Successful lifestyle intervention seems to overcome the impact of family history and genetic risk of T2DM
4. *Regarding gene-lifestyle interactions, prospective intervention studies are needed to confirm the DPS/DPP results

Elämän tähden

Healthy dietary patterns work

The New England
Journal of Medicine

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REVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

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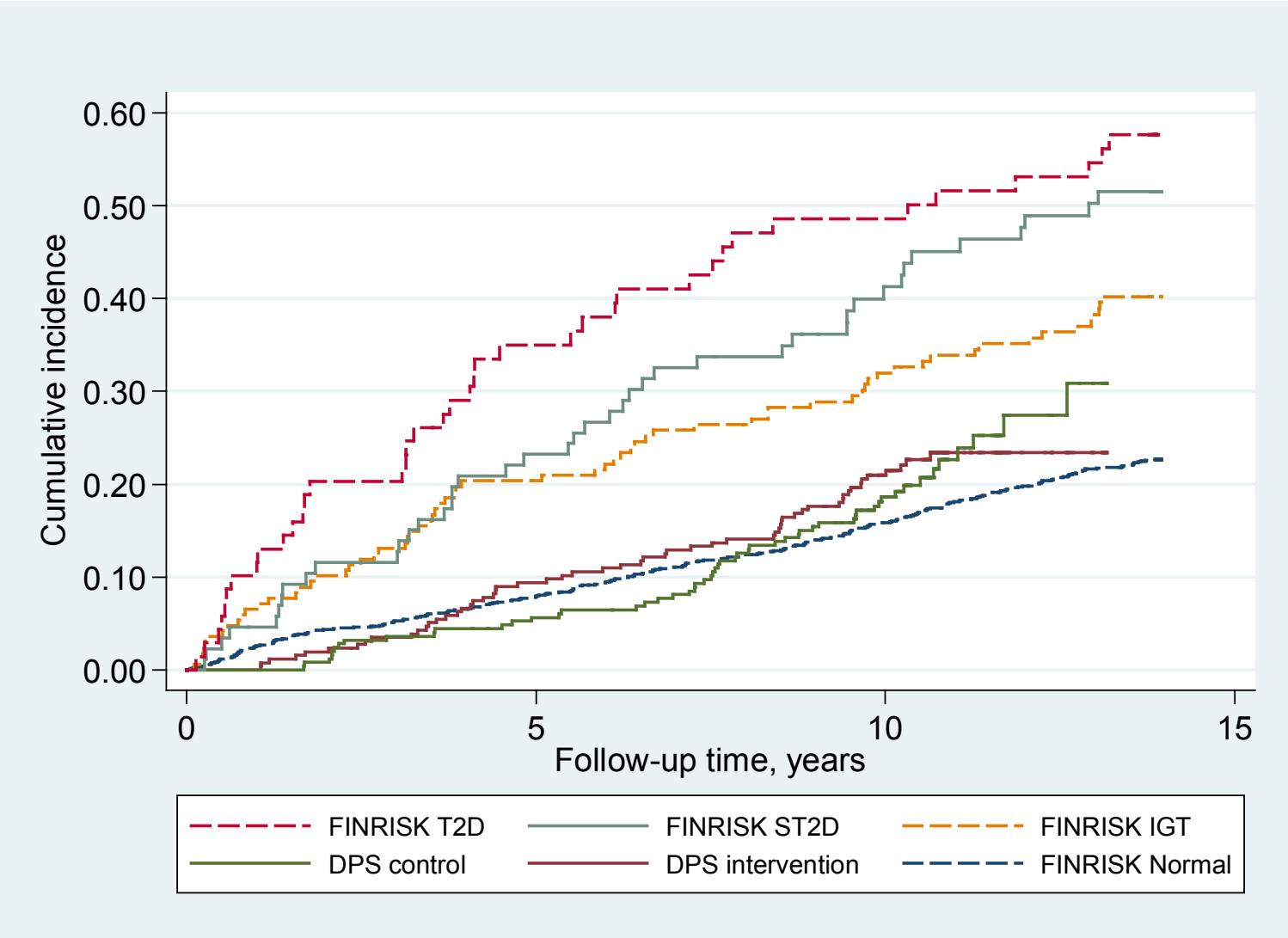
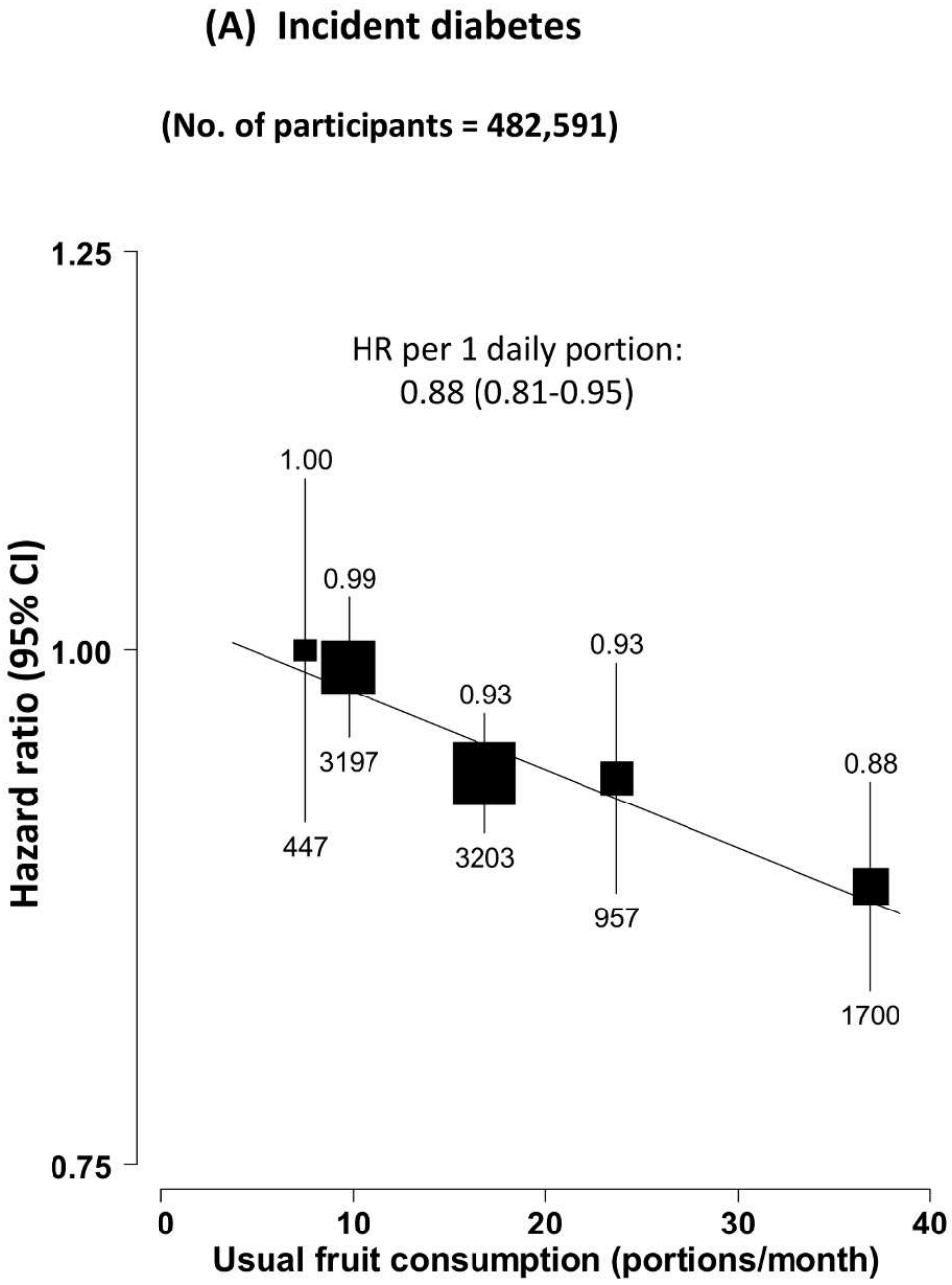
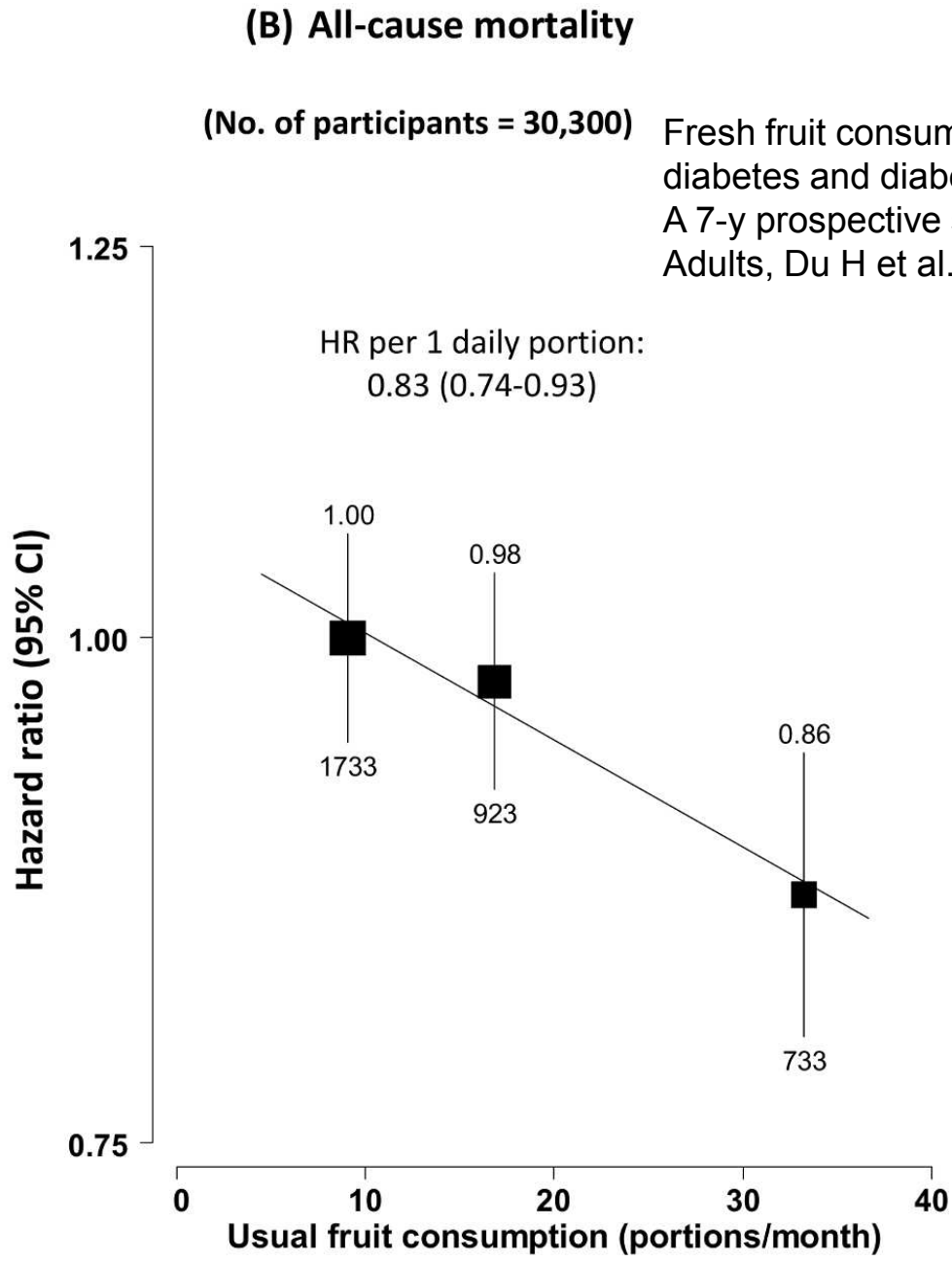
Thanks!

Figure 1. Cumulative incidence of total CVD in the DPS and FINRISK studies Uusitupa et al. PLOS One 2009







Fresh fruit consumption in relation to incident diabetes and diabetic vascular complications: A 7-y prospective study of 0.5 million Chinese Adults, Du H et al. PLoS Med 2017