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Background

- “The term ‘prediabetes’ is a practical and convenient term for impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).” [CDA 2008 Clinical Practice Guidelines]
- A meta-analysis of studies predicting risk for progression from pre-diabetes to type 2 diabetes (T2D) concluded that, compared to individuals with normoglycemia, annualized relative risks are:
 - 4.66 for those with IFG;
 - 6.35 for those with IGT;
 - 12.13 for those with both IFG and IGT. [Gerstein 2007]
- Precise data on the incidence and prevalence of pre-diabetes in Canada are not available. Estimates for 2004 were that 5 million Canadians had pre-diabetes. This number is projected to reach >6.3 million by 2016. [PHAC 2009]
- This report seeks to summarize existing evidence on pre-diabetes to assist health service providers of the Champlain LHIN address some of the challenges in caring for the pre-diabetic population, i.e.:
 - how best to leverage primary care in the screening and treatment of pre-diabetes;
 - how to reach high-risk and minority populations with pre-diabetes screening/treatment interventions;
 - how best to overcome geographic and socioeconomic challenges e.g. rural versus urban populations.

Some of the evidence in this report is highlighted in shaded boxes – these emphasize evidence from systematic reviews or expert consensus statements.

Some of the highlighted evidence comes from the type 2 diabetes literature and is labeled as such.

Is it clinically beneficial to screen patients for pre-diabetes?

Systematic Review Evidence

An AHRQ-funded systematic review failed to locate direct evidence that systematic primary care screening for T2D, IFG, or IGT among asymptomatic adults improves health outcomes. [Norris 2008]

Is it clinically beneficial to treat patients for pre-diabetes?

- An ever-growing body of evidence has demonstrated that T2D can be delayed and/or prevented in those with pre-diabetes: the Diabetes Prevention Program (DPP) [DPPRG 2009]; the Da Qing trial [Li 2008] and the Finnish Diabetes Prevention Study (DPS). [Tuomilehto 2001]
- Several large drug trials also demonstrate improvements in patients with IFG and/or IGT [e.g. DREAM, STOP-NIDDM, XENDOS]

Systematic Review Evidence

An AHRQ-funded systematic review of 11 RCTs concludes that treatment of IFG/IGT delays progression to T2D. [Norris 2008]

Which interventions are effective in screening for pre-diabetes?

- There has been debate over which diagnostic test is best: fasting plasma glucose (FPG) lacks sensitivity and specificity; oral glucose tolerance testing (OGTT) is burdensome to patients and health systems and has poor reproducibility. There has been debate among experts as to the value of the HbA1c in detecting pre-diabetes. [Kenealy 2007, Santaguida 2005]
- The CDA’s 2008 Clinical Practice Guidelines state “... the lack of standardization of the A1C test precludes its use in the diagnosis of diabetes.” [CDA 2008]

Recent International Expert Committee Consensus Statement on HbA1c

More recently however, an International Expert Committee convened to develop a consensus statement on the use of HbA1c in the diagnosis of T2D. They conclude that:

- 1. The HbA1c is the diagnostic tool of choice in diagnosing T2D.**
2. The usefulness of HbA1c in diagnosing pre-diabetes is questionable because "...the classification of subdiabetic hyperglycemia as pre-diabetes is problematic."
3. "The categorical clinical states pre-diabetes, IFG, and IGT fail to capture the continuum of risk and will be phased out of use as A1C measurements replace glucose measurements." [Int'l Expert Cmte 2009]

- A recent consensus statement from the American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE) recommends primary care diabetic screening for all patients based on identified risk factors; those determined to be high-risk should then receive a diagnostic test to establish their status. [Garber 2008]
- The FINDRISC Score is a widely used and validated risk assessment tool. [Lindstrom 2003]

Which interventions are effective in the treatment of pre-diabetes?

- As yet, there is no expert consensus on the management of pre-diabetes. [Sharma 2009]

Lifestyle interventions

Systematic Review Evidence

- A systematic review and meta-analysis of trials of lifestyle interventions for those at high-risk of developing T2D concluded that they are effective in reducing risk of developing the disease. [Yamaoka 2005]
- A Cochrane systematic review of diet-only interventions for prevention of T2D concluded that, while few RCTs have examined diet-only interventions (n=2) they are effective at reducing the risk of developing T2D. [Nield 2008]

- Two Cochrane systematic reviews of non-pharmacological interventions (dietary and/or exercise, behavioural) to prevent T2D concluded that these interventions produce a significant improvement in weight loss and incidence of the disease, but that more evidence is needed on exercise-only interventions. [Norris 2005, Orozco 2008]

Medical interventions

- There has been debate over whether medical interventions actually prevent T2D or merely mask the symptoms – the DPP study addressed this issue with a washout period after which the benefits achieved by medication were sustained. [Knowler 2002, Misra 2009]

Systematic Review Evidence

- A Cochrane systematic review and meta-analysis examined RCTs of acarbose in individuals with IFG and/or IGT. The authors conclude that "There is evidence that acarbose reduces the incidence of type 2 diabetes in patients with IGT. However, it is unclear whether this should be seen as prevention, delay or masking of diabetes." [van de Laar 2006]
- A systematic review and meta-analysis of RCTs of metformin in individuals at risk for T2D concludes that "Metformin treatment in persons at risk for diabetes improves weight, lipid profiles, and insulin resistance, and reduces new-onset diabetes by 40%." [Salpeter 2008]

- The CDA recommends metformin or acarbose for patients with IGT. For patients with IGT and/or IFG and no known CVD, thiazolidinedione is recommended. [CDA 2008]
- As yet in the US, there are no medications approved by the FDA for the treatment of pre-diabetes. [Garber 2008]

Both lifestyle and medical interventions

Systematic Review Evidence

- A systematic review and meta-analysis comparing the effectiveness of lifestyle against medical interventions for pre-diabetes concluded that they are equally as effective in reducing the risk of developing T2D. [Gillies 2007]

- A systematic review of studies examining both lifestyle and pharmacological interventions for delaying and/or preventing T2D concluded that while intervention is shown to be effective in clinical research, questions remain about the cost-effectiveness and feasibility of implementing such interventions in clinical practice. [Lauritzen 2007]

Is it cost-effective to screen and treat patients for pre-diabetes?

- In general, there is consensus that delaying and/or preventing T2D is cost-beneficial for health systems. [Bloomgarden 2008, ADA 2008, Hoerger 2007]
- Various analyses on the DPP dataset using different models have resulted in different conclusions. This has spawned debate among experts as to precisely how cost-effective lifestyle interventions for pre-diabetes truly are. [Eddy 2005, Herman 2005, Ackermann 2006]

What are some of the challenges in screening for and treating pre-diabetes?

- Systems are not in place to implement the lifestyle interventions that are known to be effective; meds may be easier for primary care physicians to distribute to patients. [Kenealy 2007]
- Interventions do not often produce the same impact when transferred from the ideal conditions of clinical research into the real-world conditions of clinical practice. [Lauritzen 2007]

Physician ambivalence: Canadian primary care context

- A 2007 series of focus groups with Canadian general/family physicians found that there is debate over the existence of pre-diabetes as a clinical entity. There is also limited and inconsistent use of the term.
 - Physicians expressed that screening for and treating pre-diabetes is not generally a priority in their practices.
 - While physicians were aware of some risk factors for pre-diabetes i.e. obesity, age, family history, they were largely unaware of other risk factors i.e. ethnic background.
 - Physicians expressed skepticism over their patients' ability or willingness to take part in lifestyle interventions for pre-diabetes.

- Among other things, study authors recommend
 - 1) CME programs on pre-diabetes
 - 2) fee codes specific to pre-diabetes
 - 3) increased awareness of the inadequacy of FPG in the diagnosis of pre-diabetes. [Ipsos-Reid 2007]

Patient ambivalence

- While generally effective for reducing IFG and IGT, lifestyle interventions are resource intensive, have limited adherence and modest success over the long-term. [Aroda 2008]

Relevant Systematic Review Evidence from the T2D literature

A systematic review of 21 studies of interventions designed to improve adherence to treatment for T2D concluded that: "Current efforts to improve or facilitate adherence of people with type 2 diabetes to treatment recommendations do not show significant effects nor harms. The question whether any intervention enhances adherence to treatment recommendations in type 2 diabetes effectively, thus still remains unanswered." [Vermeire 2005]

- A study of mediating factors behind poor adherence to lifestyle interventions for chronic disease in a general population found that diagnosis and knowledge of IGT improves acceptance of and adherence to a diet and exercise program. [Toft 2006]

Patient uncertainty

- A qualitative UK study of patients recently diagnosed with pre-diabetes found the recurring theme from interviews was that of uncertainty about their diagnosis and a need for information and support. [Troughton 2008]

Which frameworks and/or models for the screening and treatment of pre-diabetes at a population level have been described and/or trialed?

National T2D prevention programs around the world

- Finland: The FIN-D2D program is part of a large, national initiative to prevent T2D. It is an 3-pronged, national, integrated strategy that aims prevention at a population level; prevention for high-risk individuals; and early diagnosis and management of T2D [Saaristo 2007]

- **EU:** An international effort known as the IMAGE project (Development and **I**mplementation of **a** European **G**uideline and Training Standards for Diabetes prevention). The initiative aims to meet four primary objectives and implement them into primary care:
 - establishment of joint European guidelines;
 - a European training curriculum;
 - European standards for quality control of diabetes prevention programmes; and
 - a European e-health training portal. [Schwarz 2007]
- **UK:** The NHS has developed a national initiative entitled 'NHS Health Check'. The programme aims to identify individuals with, or at risk of developing heart disease, stroke, diabetes and kidney disease. Delivered through primary care, the programme aims to invite all adults ages 40-74 who have not been diagnosed with any one of the four conditions to undergo a preventive assessment. [DOH 2009]
- **Germany:** The TUMAINI model is a framework designed to effectively translate evidence on the prevention of T2D into primary health care using three main steps:
 - identify those at high risk to develop T2D;
 - short-term intensive intervention based on self-management intention principle;
 - long-term intervention to maintain motivation. [Schwarz 2007]

The International Diabetes Foundation (IDF) consensus statement on the treatment of T2D

Three steps are proposed as a framework for screening and treating populations for pre-diabetes:

- identification of risk;
- measurement of risk;
- intervention to prevent or delay progression to T2D. [Alberti 2007]

Motivational interviewing

- Motivational interviewing is a suggested technique for managing the challenge of patient ambivalence around adherence to preventive lifestyle measures. Studies with chronic disease populations suggest it is effective in producing the desired behaviour and results, and can be cost- and resource-efficient. [Biuso 2007, Rubak 2005, Roumen 2009]
- The motivational interviewing model has been studied in several populations at risk for diabetes. Results indicate that it is less resource-intensive than other lifestyle interventions for pre-diabetes

with comparable success in preventing T2D. [Greaves 2008, Penn 2009, Whitemore 2009]

Systematic Review Evidence

A systematic review and meta-analysis of RCTs of motivational interviewing interventions concludes: "Motivational interviewing in a scientific setting outperforms traditional advice giving in the treatment of a broad range of behavioural problems and diseases." [Rubak 2005]

Which strategies could the Champlain LHIN use to engage with and leverage primary care in the screening and treatment of pre-diabetes?

- Little work has been done on how best to translate the findings of effective clinical research interventions for pre-diabetes into the real-world of public health and primary care. [Crandall 2008]

In the doctor's office

- A Danish trial trained GPs in optimal management of individuals with IFG/IGT; authors conclude that, compared with controls, the trained GPs did not improve health outcomes for patients. [Rasmussen 2008]
- The GOAL trial is a "real-world" implementation study – 3yr follow up has just been published and improvements in body mass, blood glucose and other critical outcomes have been maintained. [Absetz 2009]
- Nurse Practitioner (NP) primary care practices were randomized to deliver either a more intensive or less intensive lifestyle intervention to patients at risk for diabetes – results showed that both interventions were effective in helping patients achieve weight loss. [Penn 2009]
- A large trial is underway in the Netherlands using NPs in primary care offices; patients screened as high-risk will be randomized to a cognitive behaviour program or control. Follow up will be over 2yrs. [Lakerveld 2008]
- Pilot of a primary care educational toolkit to address the information needs of pre-diabetic patients and health professionals found the intervention to be acceptable and useful to participants. The study identified 3 key messages for health professionals and pre-diabetic patients:
 1. the seriousness of the condition;
 2. the preventability of progression to diabetes;
 3. the need for lifestyle change. [Evans 2007]

Relevant Systematic Review Evidence and Commentary from the T2D literature

- “There is little good evidence for the effectiveness of primary care interventions in changing lifestyles or modifying key laboratory indicators, such as glycosylated hemoglobin (HbA1C). Most promising are multi-component strategies that combine brief advice from physicians with links to community resources including dietitians, nurses, exercise programs, and specialized diabetes education centres.” [Harris 2003]
- A systematic review of RCTs of interventions aimed at health professionals to improve process of care and/or health outcomes in patients with T2D concluded that “Multifaceted professional interventions and organizational interventions that facilitate structured and regular review of patients were effective in improving the process of care. The addition of patient education to these interventions and the enhancement of the role of nurses in diabetes care led to improvements in patient outcomes and the process of care.” [Renders 2001]

How could the Champlain LHIN engage with and leverage the community in the screening and treatment of pre-diabetes?

At the Community Health Centre

Systematic Review Evidence from the T2D literature

- A systematic review of 18 RCTs of interventions examining the effectiveness of community health workers supporting the care of people with T2D found that “There are some preliminary data demonstrating improvements in participant knowledge and behaviour.” [Norris 2006]
- A meta-analysis of studies examining self-management training for those with T2D found an inverse relationship between GHb levels of participants and the amount of time spent with an educator. [Norris 2002]

At the ‘YMCA’

- A cluster-randomized trial comparing a group-based Diabetes Prevention Program intervention versus brief individual counseling – results at 12-14mos showed statistically significant reduction in weight, BMI and total cholesterol for YMCA DPP participants [Finch 2009, Ackermann 2008]

At the Pharmacy

Systematic Review Evidence from the T2D literature

- A systematic review of trials of interventions to improve care for T2D patients using pharmacists found a significant improvement in HbA1c levels. “... due to the clinical significance of reported improvements in A1C, further trials with pharmacist case managers are warranted. Prospective assessments of the comparable efficacy of pharmacists to improve diabetes outcomes through self-management education and pharmacologic management are recommended.” [Wubben 2008]

In the workplace

- A small trial of a workplace diabetes screening and prevention program delivered by the occupational health nurse showed a significant reduction in waist circumference and improvement in IGT at 24mos follow-up. [Aldana 2006]
- A retrospective examination of occupational health records in Germany revealed that, as part of a routine exam, 5% of previously-undiagnosed employees were identified as having pre-diabetes; authors conclude that integrating T2D screening into an existing occupational health program can detect a significant number of individuals suffering from pre-diabetes. [Oberlinner 2008]
- Toronto Public Health plans to integrate diabetes prevention measures into their existing “Health Options at Work” program. [TPH Diabetes Strategy Update]

By automated telephone reminder

- A small US trial demonstrated modest improvement in the body mass of pre-diabetic patients randomized to an interactive voice response (IVR) intervention delivered via telephone. [Estabrooks 2008]

How best can the Champlain LHIN ensure that various high risk groups e.g. rural, Francophone, ethnic minority populations are reached with screening interventions for pre-diabetes?

- Canadian primary care physicians need to be made acutely aware of their role in and the importance of screening high-risk populations, as well as which groups are at greater risk. [Ipsos-Reid 2007]
- The QDScore is a newly validated T2D risk score that takes into account ethnicity and socioeconomic status (UK). It is shown to be accurate, does not require lab tests and can be self-administered in minutes. [Hippisley-Cox 2009]
- The ‘Screening for Impaired Glucose Tolerance Study’ has assessed screening performance of random plasma glucose (RPG) tests for a large cohort of individuals without known diabetes. They conclude that: “Use of age, BMI, and race/ethnicity in guidelines for screening to detect diabetes and pre-diabetes may be less important than evaluation of RPG. RPG should be investigated further as a convenient, inexpensive screen with good predictive utility.” [Zeimer 2008]

How best can the Champlain LHIN ensure that various high risk groups e.g. rural, Francophone, ethnic minority populations are reached with interventions for treating pre-diabetes?

- Cultural beliefs must be considered and addressed e.g. perceptions of overweight [Alberti 2007]
- Determination of risk-level must not rely solely on measures that have been shown effective in Caucasian populations; e.g. risk measurements such as waist circumference and BMI must take into account the individuals’ ethnic group [Alberti 2007]
- An Israeli analysis of health records and national socioeconomic data revealed that: “Individuals living in lower socioeconomic areas were less likely to have blood tests. Among tested patients, the prevalence of pre-diabetes was higher in areas of lower SES and their dietitian visits were less frequent.” [Endevelt 2009]
- Dr. Baiju Shah of the Sunnybrook Health Sciences Centre in Toronto has received funding for an exploratory study to examine diabetics of Chinese and South Asian descent to determine:
 - how they use health care;
 - how well they self-manage their diabetes;
 - whether the ethnicity of their doctor influences their care. [CDA Research Report 2008-9]

Relevant Systematic Review Evidence from the T2D literature

- A systematic review of trials of interventions to improve care among socially disadvantaged people with diabetes found: “...evidence for the effectiveness of interventions to improve diabetes care among socially disadvantaged populations and identifies key intervention features that may predict success. These types of interventions would require additional resources for needs assessment, leader training, community and family outreach, and follow-up.” [Glazier 2006]
- Another systematic review examined studies of interventions designed to address health disparities among racial and ethnic minorities with T2D. The study concludes: “There is evidence supporting the use of interventions that target patients (primarily through culturally tailored programs), providers (especially through one-on-one feedback and education), and health systems (particularly with nurse case managers and nurse clinicians).” [Peek 2007]

Conclusions

- Pre-diabetes is a significant problem in Canada and around the world.
- International experts have suggested that the term “pre-diabetes” may outlive its usefulness as understanding of the disease evolves into a risk continuum.
- Several European nations are launching ambitious population-level initiatives specifically aimed at the prevention and/or delay of T2D.
- While there is an ever-growing body of evidence on the effectiveness of screening and treatment strategies for pre-diabetes in clinical research, there is limited evidence on how best to transfer effective interventions into the ‘real-world’ of primary care and public health.
- There is a rich body of literature around the implementation of effective interventions into primary care for T2D and chronic disease.
- Lessons learned in implementation research around T2D and other chronic diseases may help inform the gaps in our understanding of implementing effective interventions for pre-diabetes into primary care and public health.

References

1. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes*. 2008;32(suppl 1): S1-S201.
2. Gerstein HC, Santaguida P, Raina P, Morrison KC, Balion C, Hunt D, Yazdi H, Booker L. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: A systematic overview and meta-analysis of prospective studies. *Diabetes Res Clin Prac* 2007; 78, 305–312.
3. Public Health Agency of Canada. Diabetes Policy Review - Report of the Expert Panel. 2009 Accessed at <http://www.phac-aspc.gc.ca/publicat/2009/dprrep-epdrg/index-eng.php> November 2009.
4. Norris SL, Kansagara D, Bougatsos C, Fu R. Screening Adults for Type 2 Diabetes: A Review of the Evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2008;148:855-868.
5. Diabetes Prevention Program Research Group, 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* 2009; 374:9702, 1677-1686.
6. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet* 2008; 371: 1783–89.
7. Tuomilehto J, Lindstro'm J, Eriksson JG, Valle TT, Ha'ma' la'inen H, Ilanne-Parikka P, Keina'nen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001 344:1343–1350
8. Gerstein HC, Yusuf S, Bosch J, et al. (DREAM [Diabetes Reduction Assessment with ramipril and rosiglitazone Medication]). Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet* 2006;368:1096–105.
9. The DREAM Trial Investigators. Rationale, design and recruitment characteristics of a large, simple international trial of diabetes prevention: the DREAM trial. *Diabetologia* 2004; 47:1519–1527 DOI 10.1007/s00125-004-1485-5. Yates T, Davies M, Khunti K. Preventing type 2 diabetes: can we make the evidence work? *Postgrad Med J* 2009;85:475–480. doi:10.1136/pgmj.2008.076166. Goldberg RB. Prevention of type 2 diabetes. *Medical Clinics of North America* 1998; 82:4, 805–821.
10. Chiasson J, Josse RG, Gomis R, et al. Acarbose for prevention of type 2 diabetes mellitus: The STOP-NIDDM randomised trial. *Lancet* 2002;359:2072–7.
11. Torgerson JS, Hauptman J, Boldrin MN, et al. XENical in the Prevention of Diabetes in Obese Subjects (XENDOS) study: A randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155–61.
12. Kenealy T, Elley CR, Arroll B. Screening for diabetes and prediabetes. *Lancet* 2007; 370, 1888-9.
13. Santaguida PL, Balion C, Hunt D, Morrison K, Gerstein H, Raina P, Booker L, Yazdi H. Diagnosis, Prognosis, and Treatment of Impaired Glucose Tolerance and Impaired Fasting Glucose. Summary, Evidence Report/Technology Assessment No. 128. (Prepared by the McMaster Evidence-based Practice Center under Contract No. 290-02-0020). AHRQ Pub. No 05-E026-1. Rockville, MD: Agency for Healthcare Research and Quality. August 2005.
14. The International Expert Committee. International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes. *Diabetes Care* 2009; 32:7, 1327-1334.
15. Garber AJ, Handelsman Y, Einhorn D, et al. Diagnosis and management of prediabetes in the continuum of hyperglycemia: when do the risks of diabetes begin? A consensus statement from the American College of Endocrinology and the American Association of Clinical Endocrinologists. *Endocr Pract* 2008, 14:933–946.
16. Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care* 2003; 26, 725–31.
17. Sharma MD, Garber AJ. What Is the Best Treatment for Prediabetes? *Current Diabetes Reports* 2009, 9:335–341.
18. Yamaoka K, Tango T. Efficacy of lifestyle education to prevent type 2 diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care* 2005; 28:11, 2780–2786.
19. Nield L, Summerbell CD, Hooper L, Whittaker V, Moore H. Dietary advice for the prevention of type 2 diabetes mellitus in adults. *Cochrane Database of Systematic Reviews* 2008, Issue 3. Art. No.: CD005102. DOI:10.1002/14651858.CD005102.pub2.
20. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Long-term non-pharmacological weight loss interventions for adults with prediabetes. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD005270. DOI:10.1002/14651858.CD005270.
21. Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roqué i Figuls M, Richter B, Mauricio D. Exercise or exercise and diet for preventing type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2008, Issue 3. Art. No.: CD003054. DOI: 10.1002/14651858.CD003054.pub3.
22. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002 346:393–403.
23. Misra A. Prevention of type 2 diabetes: the long and winding road. *The Lancet*. Published online October 29, 2009 DOI:10.1016/S0140-6736(09)61631-7.
24. van de Laar FA, Lucassen PLBJ, Akkermans RP, Van de Lisdonk EH, De Grauw WJC. Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose. *Cochrane Database of Systematic Reviews* 2006; 4:CD005061. DOI:10.1002/14651858.CD005061.pub2.
25. Salpeter SR, Buckley NS, Kahn JA, Salpeter EE. Meta-analysis: Metformin Treatment in Persons at Risk for Diabetes Mellitus. *Am J Med* (2008) 121, 149-157.
26. Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT, Khunti K. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ* 2007; doi:10.1136/bmj.39063.689375.55.
27. Lauritzen T, Borch-Johnsen K, Sandbæk A. Is prevention of Type-2 diabetes feasible and efficient in primary care? A systematic PubMed review. *Primary Care Diabetes* 2007; 1, 5–11.
28. Bloomgarden ZT. American College of Endocrinology Pre-Diabetes Consensus Conference: Part Three. *Diabetes Care* 2008; 31:12, 2404-2409.
29. American Diabetes Association. Economic costs of diabetes in the U.S. in 2007. *Diabetes Care* 2008; 31:596-615.
30. Hoerger TJ, Hicks KA, Sorensen SW, Herman WH, Ratner RE, Ackermann RT, Zhang P, Engelgau MM. Cost-Effectiveness of Screening for Pre-Diabetes Among Overweight and Obese U.S. Adults. *Diabetes Care* 2007; 30:2874–2879.
31. Eddy D, Schlessinger L, Kahn R. Clinical Outcomes and Cost-Effectiveness of Strategies for Managing People at High Risk for Diabetes. *Ann Intern Med*. 2005;143:251-264.
32. Herman WH, Hoerger TJ, Brandle M, Hicks K, Sorensen S, Zhang P, Hamman RF, Ackermann RT, Engelgau MM, Ratner RE for the Diabetes Prevention Program Research Group. The Cost-Effectiveness of Lifestyle Modification or Metformin in Preventing Type 2 Diabetes in Adults with Impaired Glucose Tolerance. *Ann Intern Med*. 2005;142:323-332.
33. Ackermann R, Hicks K, Hoerger T, Sorensen S, Zhang P, Engelgau M, Ratner R, Herman W. An Evaluation of Cost Sharing to Finance a Diet and Physical Activity Intervention to Prevent Diabetes. *Diabetes Care* 2006; 29:6
34. Ipsos-Reid Executive Summary Report to the Public Health Agency of Canada. General Practitioners' Knowledge, Attitudes and Behaviour concerning Prediabetes and Related Interventions for Prevention of Type 2 Diabetes. March 2007. Accessed at http://epe.lac-bac.gc.ca/100/200/301/pwgsc-tpsgc/por-ef/public_health_agency_canada/2007/335-06/summary.pdf November 2009.

35. Aroda VR, Ratner R. Approach to the Patient with Prediabetes. *J Clin Endocrinol Metab* 2008; 93(9):3259–3265.
36. Vermeire EIJJ, Wens J, Van Royen P, Biot Y, Hearnshaw H, Lindenmeyer A. Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD003638. DOI: 10.1002/14651858.CD003638.pub2.
37. Toft UN, Kristoffersen LH, Aadahl M, von Huth Smith L, Pisinger C, Jørgensen T. Diet and exercise intervention in a general population - mediators of participation and adherence: the Inter99 study. *European Journal of Public Health* 2006; 17:5, 455–463.
38. Troughton J, Jarvis J, Skinner C, Robertson N, Khunti K, Davies M. Waiting for diabetes: Perceptions of people with pre-diabetes: A qualitative study. *Patient Education and Counseling* 2008; 72, 88–93.
39. Saaristo T, Peltonen M, Keinanen-Kiukaanniemi S, et al. National type 2 diabetes prevention programme in Finland: FIN-D2D. *Int J Circumpolar Health*. 2007;66:101–112.
40. Schwarz PE, Schwarz J, Schuppenies A, et al. Development of a diabetes prevention management program for clinical practice. *Public Health Rep* 2007; 122, 258–63.
41. Department of Health. Putting Prevention First NHS Health Check: Vascular Risk Assessment and Management Best Practice Guidance. 2009 Accessed at http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_098410.pdf November 2009.
42. Schwarz PE, Gruhl U, Bornstein SR, Landgraf R, Hall M, Tuomilehto J. The European perspective on diabetes prevention: development and Implementation of A European Guideline and training standards for diabetes prevention (IMAGE). *Diab Vas Dis Res* 2007; 4:4, 353-357.
43. Alberti KG, Zimmet P, Shaw J. International Diabetes Federation: A consensus on type 2 diabetes prevention. *Diabet Med*. 2007;24:451–463.
44. Biuso T, Butterworth S, Linden A. A Conceptual Framework for Targeting Prediabetes with Lifestyle, Clinical, and Behavioral Management *Interventions Disease Management* 2007; 10:1, 6-15.
45. Rubak S, Sandbæk A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. *British Journal of General Practice* 2005; 55: 305–312.
46. Roumen C, Blaak E, Corpeleijn E. Lifestyle intervention for prevention of diabetes: determinants of success for future implementation. *Nutrition Reviews* 2009; 67:3, 132–146 doi:10.1111/j.1753-4887.2009.00181.x.
47. Greaves CJ, Middlebrooke A, O’Loughlin L, Holland S, et al. Motivational interviewing for modifying diabetes risk: a randomised controlled trial *Br J Gen Pract* 2008; DOI: 10.3399/bjgp08X319648.
48. Penn L, White M, Oldroyd J, Walker M, Alberti KGMM, Mathers JC. Prevention of type 2 diabetes in adults with impaired glucose tolerance: the European Diabetes Prevention RCT in Newcastle upon Tyne, UK. *BMC Public Health* 2009, 9:342 doi:10.1186/1471-2458-9-342.
49. Whittlemore R, Melkus G, Wagner J, Dziura J, Northrup V, Grey M. Translating the Diabetes Prevention Program to Primary Care: A Pilot Study. *Nursing Research* 2009; 58:1, 2-12.
50. Crandall J, Knowler W, Kahn S, Marrero D, Florez J, Bray G, Haffner S, Hoskin M, Nathan D for the Diabetes Prevention Program Research Group. The prevention of type 2 diabetes. *Nat Clin Pract Endocrinol Metab* 2008; 4: 382–93.
51. Rasmussen S, Glümer C, Sandbæk A, Lauritzen T, Borch-Johnsen K. General effect on high-risk persons when general practitioners are trained in intensive treatment of type 2 diabetes. *Scandinavian Journal of Primary Health Care* 2008; 26:3,166-173.
52. Absetz P, Oldenburg B, Hankonen N, Valve R, Heinonen H, Nissinen A, Fogelholm M, Talja M, Uutela A. Type 2 diabetes prevention in the real world: three-year results of the GOAL lifestyle implementation trial. *Diabetes Care* 2009; 32:8, 1418-20.
53. Lakerveld J, Bot SDM, Chinapaw1 MJ, van Tulder MW, van Oppen1 P, Dekker JM, Nijpels G. Primary prevention of diabetes mellitus type 2 and cardiovascular diseases using a cognitive behavior program aimed at lifestyle changes in people at risk: Design of a randomized controlled trial. *BMC Endocrine Disorders* 2008, 8:6.
54. Evans PH, Greaves C, Winder R, Fearn-Smith J, Campbell JL. Development of an educational ‘toolkit’ for health professionals and their patients with prediabetes: The WAKEUP study (Ways of Addressing Knowledge Education and Understanding in Pre-diabetes) *Diabet. Med* 2007; 24, 770–777.
55. Renders CM, Valk GD, Griffin SJ, Wagner EH, Eijk Van JT, Assendelft WJJ. Interventions to improve the management of diabetes in primary care, outpatient, and community settings: a systematic review. *Diabetes Care* 2001; 24:1821–1833.
56. Harris SB, Petrella RJ, Leadbetter W. Lifestyle interventions for type 2 diabetes: Relevance for clinical practice. *Canadian Family Physician* 2003; 49, 1618-1625.
57. Oberlinner C, Neumann SM, Ott MG, Zober A. Screening for pre-diabetes and diabetes in the workplace. *Occupational Med* 2008;58:41–45.
58. Aldana S, Barlow M, Smith R, Yanowitz F, Adams T, Loveday L, Merrill RM. Worksite Diabetes Prevention Program: Two-Year Impact on Employee Health. *American Association of Occupational Health Nurses Journal*. September 2006 54:9; 389-95
59. Toronto Public Health. Diabetes Prevention Strategy Update. Accessed at <http://www.toronto.ca/legdocs/mmis/2009/hl/bgrd/backgroundfile-18867.pdf> November 2009
60. Wubben, DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. *Pharmacotherapy* 2008; 28, 421-436.
61. Finch E, Kelly M, Marrero D, Ackermann R. Training YMCA Wellness Instructors to Deliver an Adapted Version of the Diabetes Prevention Program Lifestyle Intervention *The Diabetes Educator* 2009; 35; 224.
62. Ackermann R, Finch E, Brizendine E, Zhou H, Marrero D. Translating the Diabetes Prevention Program into the Community *The DEPLOY Pilot Study*. *Am J Prev Med* 2008;35(4):357–363.
63. Estabrooks PA, Smith-Ray RL. Piloting a behavioral intervention delivered through interactive voice response telephone messages to promote weight loss in a pre-diabetic population. *Pt Educ Couns* 2008; 72, 34–41.
64. Norris SL, Chowdhury FM, Van LK, Horsley T, Brownstein JN, Zhang X, et al. Effectiveness of community health workers in the care of persons with diabetes. *Diabetic Medicine* 2006; 23, 544-556.
65. Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes Care* 2002; 25:7,1159-1171.
66. Hippiusley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. *BMJ* 2009;338:b880.
67. Zeimer DC, Kolm P, Weintraub WS, Vaccarino V, Rhee MK, Caudle JM, Irving JM, Koch DD, Narayan KMN, Phillips L. Age, BMI, and Race Are Less Important Than Random Plasma Glucose in Identifying Risk of Glucose Intolerance *The Screening for Impaired Glucose Tolerance Study (SIGT 5)*. *Diabetes Care* 2008; 31:884–886.
68. Alberti KG. Screening and diagnosis of prediabetes: where are we headed? *Diabetes, Obesity and Metabolism*, 9 (Suppl. 1), 2007, 12–16.
69. Endevelt R, Baron-Epel O, Karpati T, Heymann AD. Does low socioeconomic status affect use of nutritional services by pre-diabetes patients? *International Journal of Health Care Quality Assurance* 2009; 22:2, 157-167.
70. Canadian Diabetes Association. The 2008-2009 Research Report. Accessed at <http://www.diabetes.ca/files/about-us/research-report-2008-2009.pdf> November 2009.
71. Glazier RH, Bajcar J, Kennie NR, Willson K. A Systematic Review of Interventions to Improve Diabetes Care in Socially Disadvantaged Populations. *Diabetes Care* 2006; 29:7, 1675-1688.
72. Peek M E, Cargill A, Huang ES. Diabetes health disparities: a systematic review of health care interventions. *Med Care Res Rev* 2007; 64:5, 101S-156S.

Other references consulted and of relevance to pre-diabetes

Commentary

- Chiasson, JL. Prevention of Type 2 diabetes: fact or fiction? *Exp Op Pharmacotherapy* 2007 8:18; 3147-3158.
- Yates T, Davies M, Khunti K. Preventing type 2 diabetes: can we make the evidence work? *Postgrad Med J* 2009;85:475–480.

Screening interventions

- Aekplakorn W, Bunnag P, Woodward M, Sritara P, Cheepudomwit S, Yamwong S. A risk score for predicting incident diabetes in the Thai Population. *Diabetes Care* 2006; 29: 1872–1877.
- Allen P, Thompson JL, Herman CJ, Qualls C, Helitzer DL, Whyte AN, et al. Impact of periodic follow-up testing among urban American Indian women with impaired fasting glucose. *Prev Chronic Dis* 2008;5(3).
- American Diabetes Association. Diabetes Risk Test. Available from: <http://www.diabetes.org/diabetes-basics/prevention/diabetes-risk-test/> (accessed November 2009).
- Canadian Diabetes Association. Are you at risk? <http://www.diabetes.ca/Files/are-you-at-risk.pdf> (accessed November 2009)
- Christensen JO, Sandbaek A, Lauritzen T, Borch-Johnsen K. Population-based stepwise screening for unrecognised Type 2 diabetes is ineffective in general practice despite reliable algorithms. *Diabetologia* 2004; 47:9, 1566–1573.
- Griffin SJ, Little PS, Hales CN, Kinmonth AL, Wareham NJ. Diabetes risk score: towards earlier detection of type 2 diabetes in general practice. *Diabetes Metab Res Rev* 2000; 16: 164–171.
- Heikes K, Eddy D, Arondekar B, Schlessinger L. Diabetes Risk Calculator: A simple tool for detecting undiagnosed diabetes and pre-diabetes *Diabetes Care* 2008; 31:1040–1045.
- Schwarz PE, Li J, Lindstrom J, Tuomilehto J. Tools for predicting the risk of type 2 diabetes in daily practice. *Horm Metab Res* 2009;41:86-97.
- Waugh N, Scotland G, McNamee P, et al. Screening for type 2 diabetes: literature review and economic modelling. *Health Technol Assess* 2007; 11.

Treatment interventions

- Daniel M, Green LW, Marion SA et al. Effectiveness of community-directed diabetes prevention and control in a rural Aboriginal population in British Columbia, Canada. *Soc Sci Med* 1999; 48, 815–832.
- Gucciardi E, DeMelo M, Lee RN, Grace SL. Assessment of two culturally competent diabetes education methods: Individual versus individual plus group education in Canadian Portuguese adults with type 2 diabetes. *Ethnicity & Health* 2007; 12:2, 163-187.
- 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* 1997 20:537–54.
- Simmons D, Rush E, Crook N on behalf of the Te Wai o Rona: Diabetes Prevention Strategy Team. Development and piloting of a community health worker-based intervention for the prevention of diabetes among New Zealand Maori in Te Wai o Rona: Diabetes Prevention Strategy. *Public Health Nutrition*: 11(12), 1318–1325 doi:10.1017/S1368980008002711.

Cost-effectiveness studies

- Josse RG, McGuire AJ, Saal GB. A review of the economic evidence for acarbose in the prevention of diabetes and cardiovascular events in individuals with impaired glucose tolerance *Int J Clin Pract* 2006; 60:7, 847–855.

Consensus statements/guidelines

- Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, Zinman B. ADA Consensus Statement: Impaired Fasting Glucose and Impaired Glucose Tolerance: Implications for care. *Diabetes Care* 2007; 30:3, 753-759.