Tool for Linking Evidence Reviews to Organizational Guideline Planning

Accompanies Methods Report: Linking Evidence Reviews to Organizational Guideline Planning: A Pilot Test of an Interactive, Web-Based Presentation and Discussion of Evidence

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Understanding the Evidence for Medication and Lifestyle Interventions to Delay the Onset of Diabetes

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The speakers have no conflicts of interest to report.
Genesis and purpose of this seminar

- AHRQ-funded effort to try to improve the uptake/use of evidence reports conducted by Evidence-based Practice Centers (EPC) by health care delivery systems
  - Joint effort with KPRA EPC, RAND EPC and KP CMI
- Interactive format to link reviews (evidence reviewers) to a broad range of stakeholders within KP—those developing clinical guidance and those implementing clinical guidance
- This seminar consists of a brief evidence presentation with ample time for discussion
Systematic review of interest

**Evidence Synthesis**

**Number 117**

**Screening for Abnormal Glucose and Type 2 Diabetes Mellitus: A Systematic Review to Update the 2008 U.S. Preventive Services Task Force Recommendation**

AHRO Publication No. 13-05190-EF-1
April 2015


Why screen?

- USPSTF recommendation to screen for DM hinges on ability of lifestyle interventions to prevent/delay the onset of DM
  - Intensive lifestyle interventions to prevent the development of diabetes consistently show a moderate benefit in reducing the progression to diabetes.

- Direct evidence that preventing a diagnosis or early identification of diabetes results in improved patient health outcomes is limited.
Key Question 7 in the systematic review

Do interventions for impaired fasting glucose or impaired glucose tolerance delay or prevent progression to type 2 diabetes?

- Lifestyle interventions
- Medications
  - e.g., metformin, thiazolidinediones, alpha-glucosidase inhibitors
As you listen to the evidence today…

- How effective are interventions to delay or prevent the onset of diabetes?
  - Do the benefits of these interventions outweigh the harms?
- What evidence do you need that is NOT covered in this systematic review?
  - What else do you need to know that is not addressed?
## Overall Findings for Key Question 7

<table>
<thead>
<tr>
<th></th>
<th>No. studies</th>
<th>Summary of findings on progression to diabetes</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lifestyle</strong></td>
<td>10</td>
<td>RR 0.57 (95% CI 0.43, 0.70)</td>
<td>Clinical heterogeneity</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>3</td>
<td>RR 0.69 (95% CI 0.49, 0.76)*</td>
<td>Few studies, TZD high statistical heterogeneity</td>
</tr>
<tr>
<td>TZD</td>
<td>3</td>
<td>RR 0.51 (95% CI 0.23, 1.06)</td>
<td></td>
</tr>
<tr>
<td>α-gluc inhibitors</td>
<td>4</td>
<td>RR 0.65 (95% CI 0.44, 0.91)</td>
<td></td>
</tr>
<tr>
<td><strong>Multifactorial interventions</strong></td>
<td>2</td>
<td>No pooled analysis, no effect on progression to DM</td>
<td>Clinical heterogeneity, Imprecision</td>
</tr>
</tbody>
</table>

* from DPP trial, no pooled estimate calculated
What is the evidence on lifestyle interventions to prevent the onset of diabetes?
Lifestyle interventions: Overlap with the review for the CDC Community Guide (Balk et al., 2015)

Reasons for non-overlap include:

- Mismatch of review’s search dates
- Study design
- Setting less relevant to US
- Error


## Results for lifestyle interventions

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Participants, n</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPP, 2002*</td>
<td>2161</td>
<td>0.50 [0.42, 0.59]</td>
</tr>
<tr>
<td>Katula, 2013</td>
<td>301</td>
<td>0.36 [0.12, 1.11]</td>
</tr>
<tr>
<td>Kosaka, 2005*</td>
<td>458</td>
<td>0.32 [0.10, 1.01]</td>
</tr>
<tr>
<td>Li, 2004</td>
<td>568</td>
<td>0.81 [0.74, 0.88]</td>
</tr>
<tr>
<td>Lindahl, 2009</td>
<td>168</td>
<td>0.20 [0.10, 0.65]</td>
</tr>
<tr>
<td>Penn, 2009</td>
<td>102</td>
<td>0.45 [0.17, 1.22]</td>
</tr>
<tr>
<td>Ramachandran, 2006*</td>
<td>253</td>
<td>0.71 [0.54, 0.94]</td>
</tr>
<tr>
<td>Saito, 2011</td>
<td>641</td>
<td>0.65 [0.43, 0.97]</td>
</tr>
<tr>
<td>Sakane, 2011</td>
<td>296</td>
<td>0.51 [0.24, 1.11]</td>
</tr>
<tr>
<td>Tuomilehto, 2001*</td>
<td>522</td>
<td>0.44 [0.29, 0.68]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>5470</td>
<td>0.53 [0.39, 0.72]</td>
</tr>
</tbody>
</table>

*From prior report

What is the evidence on medications other than metformin to prevent the onset of diabetes?
Results for TZD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Participants, n</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeFronzo, 2011</td>
<td>602</td>
<td>0.30 [0.17, 0.52]</td>
</tr>
<tr>
<td>DREAM, 2006*</td>
<td>5209</td>
<td>0.43 [0.37, 0.48]</td>
</tr>
<tr>
<td>Ramachandran, 2009</td>
<td>367</td>
<td>0.94 [0.69, 1.28]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>6238</strong></td>
<td><strong>0.60 [0.27, 0.92]</strong></td>
</tr>
</tbody>
</table>

*From prior report

Adapted from "Figure S. Meta-Analysis of the Effect of Thiazolidinediones on Incidence of Progression to DM". Source: Selph S, Dana T, Bougatsos C, Blazina I, Patel H, Chou R. Screening for Abnormal Glucose and Type 2 Diabetes Mellitus: A Systematic Review to Update the 2008 U.S. Preventive Services Task Force Recommendation. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Apr. Report No.: 15-05190-EF-1. PMID: 25973510
# Results for alpha-glucosidase inhibitors

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Participants, n</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chisaron, 2002*</td>
<td>1368</td>
<td>0.78 [0.68, 0.90]</td>
</tr>
<tr>
<td>Kawamori, 2009</td>
<td>1778</td>
<td>0.46 [0.34, 0.64]</td>
</tr>
<tr>
<td>Nipels, 2008</td>
<td>118</td>
<td>0.76 [0.38, 1.53]</td>
</tr>
<tr>
<td>Pan, 2003*</td>
<td>252</td>
<td>0.59 [0.24, 1.46]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>3516</strong></td>
<td><strong>0.64 [0.45, 0.90]</strong></td>
</tr>
</tbody>
</table>

*From prior report

Adapted from 'Figure 8. Meta-Analysis of the Effect of Alpha-Glucosidase Inhibitors on Incidence of Progression to DM'. Selph S, Dana T, Bougatsos C, Bazzini I, Patel H, Chou R. Screening for Abnormal Glucose and Type 2 Diabetes Mellitus: A Systematic Review to Update the 2008 U.S. Preventive Services Task Force Recommendation. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Apr. Report No.: 15-0510E1-1. PMID: 25993510
None of the reviews examine harms of these interventions

While lifestyle interventions don’t have any hypothesized harms, there is a cost and opportunity cost trade-off

An examination of harms of medications is necessary to assess the net benefit for these medications (particularly their long term use) to determine their role in diabetes prevention
As you listen to the implementation issues around lifestyle interventions…

- How far do you want to extrapolate from the evidence?
  - What sort of lifestyle interventions should we be offering our members?
  - Who should be offered intensive lifestyle interventions?
- What else do you want to know?
Implementation issues for lifestyle interventions - DPP as the exemplar

- Intervention goals
- Comparison group
- Training required
- Mode of delivery
- Intensity of intervention (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- Goals: achieve and maintain weight reduction ≥7% of initial body weight through a healthy low-calorie, low-fat diet and engage in moderate-intensity physical activity for ≥150 min/wk
- Participants taught to record diet and exercise.
- Offered supervised exercise sessions twice per week for duration of intervention (not mandatory).
- Intervention “flexible” culturally sensitive. Lifestyle advice was tailored to the individual with emphasis on self-esteem, empowerment, and social support.
Implementation issues for lifestyle interventions - DPP as the exemplar

- Intervention goals
- Comparison group
- Training required
- Mode of delivery
- Intensity of intervention (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- Intervention 2: standard lifestyle recommendations + metformin 850 mg PO BID.
- Control: standard lifestyle recommendations + placebo pill.
- Standard lifestyle recommendations included written information with annual 20-30 minute individual session emphasizing healthy lifestyle (diet and exercise).
Implementation issues for lifestyle interventions-
DPP as the exemplar

- Intervention goals
- Comparison group
- **Training required**
- Mode of delivery
- Intensity of intervention (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- Primary care provider for recruitment only.
- Program and recruitment coordinators that were trained in motivational interviewing.
- Case manager with training in nutrition, exercise, or behavior modification (details not reported).
- Supervised exercise leader not defined.
Implementation issues for lifestyle interventions - DPP as the exemplar

- Intervention goals
- Comparison group
- Training required
- Mode of delivery
- Intensity of intervention (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- Face to face visits (individual and group).
Implementation issues for lifestyle interventions-
DPP as the exemplar

- Intervention goals
- Comparison group
- Training required
- Mode of delivery
- Intensity of intervention (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- A case manager taught 16 one-on-one sessions over 24 weeks using a curriculum which followed the Food Guide Pyramid.
- **Subsequent sessions** led by the case manager were **monthly** and either individual or group focused on behavior reinforcement.
- 6 months core curriculum 1.8-4.6 years maintenance (mean 2.8 years).
- Optional supervised exercise sessions up to twice per week throughout intervention.
- Semiannual FBG and annual 2 hr oral glucose tolerance test.
Implementation issues for lifestyle interventions -
DPP as the exemplar

- Intervention goals
- Comparison group
- Training required
- Mode of delivery
- Intensity of intervention
  (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- Written material: Lifestyle Manuals of Operation
  (www.bsc.gwu.edu/dpp).
- Modified Block Food-Frequency Questionnaire.
- Modified Activity Questionnaire.

Lifestyle Manuals of Operation. Copyright 1996; 2011;
University of Pittsburgh.
Implementation issues for lifestyle interventions - DPP as the exemplar

- Intervention goals
- Comparison group
- Training required
- Mode of delivery
- Intensity of intervention (when and how much)
- Availability of materials
- Target population
  - setting, adherence

- **Volunteer** participants recruited through 27 (academic) US medical centers.
- **Prediabetics**: participant characteristics included being 25 years or older, BMI of 24 or more (22 or higher in Asians) and fasting plasma glucose of 95-125 or glucose of 140-199, 2 hrs after 75g glucose challenge.
- Adherence and retention actively fostered and used quarterly newsletters.
- 50% of the intervention group achieved weight loss goal by 24 weeks, 74% met exercise goal by 24 weeks, 72% took at least 80% of the prescribed dose of metformin.
What do we know about virtual interventions from the systematic reviews?

- Limited evaluations of different virtual interventions
  - NO trials reported on diabetes incidence as an outcome, all with shorter term follow-up
  - Most informative trial evaluated face-to-face vs DVD-based intensive lifestyle intervention (12+ sessions)
    - Generally high income volunteers, SF Bay area
    - At 15 months, slightly larger effects on weight loss for in person than virtual, but both more than usual care group
  - 2 comparative effectiveness trials evaluated virtual interventions (reality TV, internet) versus enhanced programs (with virtual counseling/interaction), found that enhanced programs resulted in weight loss at 12 months
Conclusions from the systematic reviews

- USPSTF recommendation to screen for DM hinges on ability of lifestyle interventions to prevent/delay the onset of DM
- Using the Balk review for CDC is reasonable, more comprehensive to the USPSTF review, consistent with USPSTF review findings for lifestyle interventions
- Understanding the details of interventions is key to reproducing intervention, as deviations from the tested intervention may result in different outcomes (effectiveness) in practice
- Understanding the harms of longer term use of medications is important before implementation
The YMCA Diabetes Prevention Program is for overweight adults (18+) with prediabetes, confirmed via one of 3 blood tests or has 2 or more risk factors.

The 12 month program (includes a 16 session core program followed by monthly maintenance sessions). Sessions are one hour per week and include 8 to 15 people in a group based, classroom setting.

Classroom-type settings allow for sessions to be conducted anytime or anywhere.

Participants weigh in at each session, their weight is recorded in an online tracking system, and the sessions are facilitated by a Y Lifestyle Coach (a person who is skilled in Listen First and group facilitation).

Health Care Innovation Award

Health Care Innovation Award (HCIA) to The Young Men’s Christian Association (YMCA) of the USA (Y-USA).


Session Attendance
• 83% ≥4
• 63% ≥9 or more

https://innovation.cms.gov/initiatives/Health-Care-Innovation-Awards/

YMCA program results

- Among the 5,696 Medicare beneficiaries who attended four or more sessions, there was a mean weight loss of 5.27 kg (~5% loss of initial weight)
- Compared to a matched cohort of 65+ pre-diabetic individuals in the same county (who did not enroll in DPP)
  - Medicare savings
  - Significantly fewer inpatient admissions and ED stays

Proposed Beneficiary Eligibility

- **Must meet Body Mass Index (BMI) Criteria:**
  - ≥ 25 (≥ 23 for Asian beneficiaries)

- **Must have Blood Test Results:**
  Have within the 12 months prior to the first core session:
  - Hemoglobin A1c of 5.7–6.4%; or
  - Fasting plasma glucose of 110–125 mg/dL; or
  - Two-hour plasma glucose of 140–199 mg/dL

- **No previous diagnosis of diabetes (gestational diabetes is allowable) or End-Stage Renal Disease (ESRD).**

Program requirements:

- Minimum 16 core sessions in first 6 months
- Monthly maintenance sessions, second 6 months
- Monthly maintenance sessions for up to 2 years

Virtual sessions—CMS policy

- (Year 1) A supplier may offer no more than 4 virtual make-up sessions within the core services period to an MDPP beneficiary,
  - of which no more than 2 virtual make-up sessions may be core maintenance sessions

- (Years 2, 3) A supplier may offer no more than 3 virtual make-up sessions that are ongoing maintenance sessions to an MDPP beneficiary during any rolling 12-month time period.

- Weights can only be recorded in-person

Discussion Questions—Implementation

- What type of lifestyle interventions should be made available?
- To whom should these lifestyle interventions be made available?

Early insights:
- Dr.’s Fitzpatrick and Fortmann, researchers at KPCHR in Portland—evaluation study to understand the implementation of virtual and in-person diabetes prevention programs at KPNW
Discussion Questions—Implementation

- When should metformin be offered or initiated?
- Are there medications other than metformin that may be reasonable to consider as prevention?