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Interventions for prevention of type 2 diabetes in relatives: A systematic review

1 Interventions for prevention of type 2 diabetes in relatives: A systematic review

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7 **Abstract**

8 The relatives and partners of people with type 2 diabetes are at increased risk of developing type 2
9 diabetes. This systematic review examines randomized controlled trials, written in English that
10 tested an intervention, which aimed to modify behaviors known to delay or prevent type 2 diabetes,
11 among the relatives or partners of people with type 2 diabetes. Study quality was assessed using the
12 Cochrane Collaboration's tool for assessing risk of bias. Seven studies met the inclusion criteria. The
13 majority of studies were at low risk of bias. Six studies tested an intervention in first-degree relatives
14 of people with type 2 diabetes and one in partners. Intervention components and intervention
15 intensity across studies varied, with those targeting diet and physical activity reporting the most
16 significant changes in primary outcomes. Only one study did not observe significant changes in
17 primary outcomes. There were three main recruitment approaches: advertising in the community,
18 recruiting people through their relatives with diabetes, or identifying people as high risk by screening
19 of their own health care contacts. Some evidence was found for potentially successful interventions
20 to prevent type 2 diabetes among the relatives and partners of people with type 2 diabetes,
21 although finding simple and effective methods to identify and recruit them remains a challenge.
22 Future studies should explore the effect of patients' perceptions on their family members' behavior
23 and capitalize on family relationships in order to increase intervention effectiveness.

24

25 **Introduction**

26 First-degree relatives of people with type 2 diabetes are at increased risk of developing this
27 condition, with offspring and siblings at a three-fold higher risk than the general population [1, 2, 3].
28 This increased risk has genetic and environmental components, the latter likely arising from shared
29 risk factors such as sedentary lifestyle, physical inactivity and obesity [4]. Co-habiting partners are
30 also at high risk from these shared risk factors [5]. Prevention studies in people at high risk provide
31 compelling evidence that type 2 diabetes can be prevented or delayed with lifestyle modifications,
32 such as increase in physical activity and healthy diet, and weight loss [6 -10]. Identifying and
33 intervening in the relatives of people with type 2 diabetes is important and could therefore form
34 part of an effective diabetes prevention strategy [11-13].

35 For diabetes prevention among relatives and partners of people with type 2 diabetes to form part of
36 such an intervention strategy, the feasibility of identifying and recruiting these high-risk people
37 needs to be established. In terms of intervention effectiveness, only one narrative review to date
38 has synthesized evidence on interventions to reduce the risk of type 2 diabetes in people with a
39 family history [7]. This review included studies of different designs, but it did not assess study quality
40 and neither did it synthesize evidence relating to partners of people with this condition. The authors
41 concluded that health promotion in people with family history of type 2 diabetes is under-
42 researched and family history is rarely used to initiate or promote behavior change. The current
43 systematic review therefore examines published randomized-controlled trials (RCTs) in order to
44 identify successful recruitment and intervention strategies for type 2 diabetes prevention in relatives
45 and partners of people with type 2 diabetes.

46

47

48 **Methods**

49 Search strategy and information sources

50 The selected databases were MEDLINE, PsychINFO, CINAHL, ASSIA and ProQuest and search terms
51 included “random* control* trial*”, “RCT”, “type 2 diabetes”, “non-insulin dependent diabetes”,
52 “NIDDM”, “family+”, “spouse*”, “partner*”, “sibling*”, “parent*” and “offspring*”. All databases were
53 searched from inception until August 2016. The reference lists of all included studies were then
54 searched by hand to identify any additional relevant studies.

55 Study selection

56 RCTs were included if they aimed to modify behaviors known to delay or prevent type 2 diabetes
57 (e.g. physical activity, healthy diet) that were delivered to the relatives and/or partners of people
58 with type 2 diabetes. Studies were excluded if they were not RCTs, if they were feasibility studies or
59 protocols, or if the participants did not have a relative/partner with type 2 diabetes (or if this was
60 not reported). Inclusion/exclusion criteria were applied in a two-step process, screening titles and
61 abstracts before screening full text (Figure 1). The search identified one trial, which was delivered to
62 patients but explored the indirect intervention effect on the patients’ partners [14]. A decision was
63 made to include the study, as partners of people with type 2 diabetes are at increased risk of type 2
64 diabetes and they remain understudied. The additional hand search through the reference lists of
65 included articles identified a narrative review [12] that led to the addition of one study not identified
66 by the initial search strategy [15-18]. Although not an RCT, this study was included as participants
67 were randomized into treatment groups through the process of minimization [19]. Minimization is
68 based on the principle of randomization although participants are allocated to treatment groups on
69 the basis of specific characteristics such as gender or BMI. This method is appropriate for controlled
70 trials with small samples because it minimizes the imbalance between different factors [19].

71

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72 *Insert figure 1 here*

73 Data extraction was carried out by ED, with included studies then checked against inclusion criteria
74 by AM. Information was collected on author and year, population sample, recruitment methods,
75 intervention components and mode of delivery, intervention duration and study outcomes.
76 Intervention components were classified according to the Behavior Change Taxonomy [20]. This was
77 done independently by two of the authors (ED and AM).

78 Assessment of study quality

79 Study quality was assessed using the Cochrane Collaboration's tool for assessing risk of bias [21]. The
80 tool allows the researcher to assess risk of bias across several domains and provides a systematic and
81 transparent method of assessing the internal validity of a study [21]. Assessors are required to assign
82 "high risk", "low risk" or "unclear risk" of bias, based on the sources of bias, which include random
83 sequence generation, allocation concealment, blinding of participants and personnel, blinding of
84 outcome assessment, incomplete outcome data and selective reporting. The tool also provides an
85 opportunity to assess bias, based on other sources that assessor considers to be relevant [21].

86 **Results**

87 Summary of studies

88 Seven studies, published in 14 articles in peer-reviewed journals, were included (Table 1). The
89 majority were published between 2000 and 2015 with only one study published prior to this (1998).
90 The studies were carried out in various geographical locations (two in the USA [14, 22]; two in the
91 Netherlands [23, 24-26]; and one each in Japan [27], Sweden [15-18] and the UK [28-30]).
92 Interventions were delivered to parents and siblings of people with type 2 diabetes [24-26, 27],
93 offspring only [22, 28-30], first degree relatives (relationships not specified) [15-18, 23] or partners
94 [14].

95 Recruitment strategies

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96 There were three main recruitment approaches: advertising in the community, recruiting people
97 through their relatives with diabetes, or identifying people as high risk (as defined by having a
98 relative with diabetes) when they had a health care contact. Three of the studies provided
99 insufficient information to assess participation rate and response [15-18, 24-26]. In the ProActive
100 trial, only 365 (24%) relatives were recruited from a pool of 1,521 trial participants [28-30]. In the
101 LookAHEAD trial, 357 (7%) partners were recruited from 5,145 trial participants [14]. In the other
102 two studies, 53% [23] and 40% [27] of eligible relatives identified through their own health care
103 contacts agreed to take part. However, one study did not state how many people needed to be
104 screened in order to identify eligible people [27]; in the other there was an initial population
105 screening of over 11,000 people [31].

106

107 Intervention components and mode of delivery

108 The interventions generally incorporated lifestyle interventions focusing on diet and/or physical
109 activity, and behavioral strategies (e.g. goal setting, self-monitoring) that were group and/or
110 individually based, with one study exploring the communication of familial risk [23]. The most often
111 used behavior change strategies [20] were “provide information on consequences”, “prompt specific
112 goal setting” and “prompt self-monitoring of behavior”.

113 Studies were too heterogeneous in terms of intervention components to allow for a meta-analysis to
114 be conducted.

115 Two studies delivered an intervention in a group environment that included information about diet,
116 exercise or a combination of both [15-18, 22]. Wing et al.’s [22] trial was the most intensive
117 intervention trial, consisting of three intervention arms and a control arm, utilizing 12 behavior
118 change strategies and lasting two years. Participants in all intervention groups attended frequent
119 meetings, which contained information about diet, exercise or both (depending on intervention

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120 group). Brekke et al.'s [15-18] intervention consisted of two intervention arms and a control and
121 incorporated 7 behavior change strategies. The intervention arms included the provision of dietary or
122 dietary and exercise advice. Participants attended two group meetings, which were followed by
123 unannounced phone calls every 10 days for four months.

124 Three studies delivered the intervention to individuals [23, 27, 28-30]. The ProActive trial [28-30]
125 compared the efficacy of an intervention delivered either in person or over the phone, using 10 key
126 ingredients from the behavior change taxonomy. The intervention lasted 12 months and focused on
127 behavioral strategies such as goal setting, action planning, self-monitoring and building support from
128 family and friends. In Pijl et al.'s [23] trial, participants attended one meeting where they were
129 informed of their genetic risk of type 2 diabetes thus the trial used only two behavior change
130 techniques Tokunaga-Nakawatase et al.'s [27] intervention was the least intensive intervention
131 identified, using three key ingredients and comprising of the provision of tailored, concrete lifestyle
132 recommendations via email in addition to a pamphlet about general diabetes prevention.

133 Two studies used a combination of group and individual mode of delivery [14, 24-26]. The
134 LookAHEAD trial [14] was the only intervention that was delivered to patients with type 2 diabetes
135 but aimed to explore its indirect effect on the patients' spouses. The intervention utilized five
136 behavior change techniques, lasted one year and included several group and two individual meetings
137 where participants received training in behavioral strategies (e.g. self-monitoring; goal setting) and
138 ways to enhance social support. The intervention in the DiAlert trial [24-26] consisted of two
139 interactive group sessions, which focused on risk factors of type 2 diabetes, the importance of
140 lifestyle changes and behavioral strategies, utilizing eight behavior change techniques. In addition,
141 participants were sent four newsletters, 1, 4, 19 and 28 weeks after the intervention, providing
142 information about healthy eating and physical activity.

143 Study quality

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144 The quality of studies was assessed using the Cochrane Collaboration's tool for assessing risk of bias
145 [21]. The results of assessment of bias are presented in Table 2.

146 *Insert table 2 here*

147 Three of the studies were at high risk of bias in one [22], two [24-26] or three domains [27], including
148 lack of blinding, incomplete outcome data and selective reporting. While there were no obvious
149 sources of bias in the other four studies, the presence of unclear risk in at least one domain for each
150 of them indicates that many studies fail to provide sufficient information for bias to be adequately
151 assessed.

152

153 Study outcomes

154 The outcomes and intervention effectiveness varied across studies. Five of the seven studies
155 reported significant changes in primary outcomes. One study reported intervention effectiveness
156 during the duration of the intervention but not thereafter [27], and one did not report significant
157 changes in study outcomes [28-30].

158 Two studies demonstrated that a combination of diet and exercise information leads to most
159 significant sustained changes in participants' behavior [15-18, 22]. Participants in the diet group in
160 Wing et al.'s [22] study reported significant decrease in daily calorie intake and weight, which was
161 sustained for a year. The diet plus exercise intervention led to increased physical activity and
162 significant weight loss, which was maintained for two years. However, the study also showed a
163 significant difference in session attendance between groups, which may have affected the results.
164 Brekke et al. [15-18] reported significant decrease in body weight, waist circumference and sagittal
165 diameter in the diet plus exercise group, compared to the control group. Within group differences
166 were observed in energy intake in the diet group and frequency of physical activity in the diet plus

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167 exercise group. Although the strength of these changes diminished, they were maintained two years
168 after the intervention.

169 Gorin et al. [14] found significant correlations between the behavior of patients and their spouses,
170 demonstrating an indirect intervention effect on the behavior of spouses of patients with type 2
171 diabetes.

172 Participants in the intervention group in Pijl et al.'s [23] study reported increased perception of
173 diabetes consequences and diabetes control. However, their behavioral intentions did not differ
174 from the intentions of participants in the control group. Significantly more participants in the
175 intervention group in the DiAlert trial [24-26] lost at least 5% of their initial body weight at 9-months
176 follow-up. However, the intervention did not affect health behaviors, intention to change behavior,
177 self-efficacy and outcome expectancies. In addition, the results did not show significant changes in
178 diet, physical activity, smoking or alcohol intake. The results from the DiAlert trial [24-26] should be
179 interpreted with caution as the study was at high risk of bias for not concealing treatment allocation
180 and anthropometric measurements from trainers and participants, for not providing an objective
181 assessment of intervention fidelity and for being underpowered.

182 One study reported intervention effectiveness during the duration of the intervention but not
183 thereafter [27]. Although changes in total energy intake were observed between the groups at 6
184 months, there were no significant differences in energy intake, physical activity or biomedical factors
185 at 12 months after the intervention. However, the results from this study should be interpreted with
186 caution as the study was considered to be at high risk of bias for selective reporting, lack of
187 explanation for missing data and not blinding participants to study group.

188 The intervention in the ProActive [28-30] did not lead to significant changes in weight, BMI, waist
189 circumference, blood pressure or cholesterol. At 1 year follow-up, the physical activity of
190 participants in the intervention groups did not differ from the physical activity of participants in the
191 control group. Although both modes of intervention delivery (over the phone and face-to-face) were

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192 considered acceptable by participants, there was no difference in study outcomes between the two
193 intervention groups.

194

195 **Discussion**

196 This systematic review shows that there has been limited research evaluating interventions that
197 target modifiable risk factors for type 2 diabetes in relatives and partners of people with type 2
198 diabetes. This is particularly true for partners. Given that theories such as Common dyadic coping
199 [32], Communal coping [33] and Family Systems Theory [34] suggest that couples and families
200 appraise illness as a joint problem that requires joint actions, there is a need to further explore how
201 the relationship between the patient and their significant others can be used as a mediator for
202 behavior change, as has been done in cancer [35]. One study in this review showed a significant
203 correlation between the behavior of patients and their spouses, which leads to behavior changes in
204 the untreated [14]. The study highlights the potential of utilizing communication in families as a
205 potential tool for prevention of type 2 diabetes. Previous research shows that people with type 2
206 diabetes are willing to inform their relatives about familial risk of diabetes [36] and that patients
207 often do that without formal prompting from healthcare professionals [37]. Additionally, van Esch et
208 al. [38] found a link between patients' perceptions of type 2 diabetes and perceptions of diabetes
209 threat in their family members. More specifically, patients who perceived type 2 diabetes as a
210 serious and unpredictable disease were more likely to be worried about their relatives' risk of type 2
211 diabetes [38]. These findings outline the characteristics of patients who may be more likely to act as
212 health educators in their families. These people can be provided with information about type 2
213 diabetes by healthcare professions, which they can then disseminate within their families. The
214 potential of such an indirect diabetes prevention strategy is further supported by previous findings
215 that relatives of people with type 2 diabetes would like to be informed about their diabetes risk [39]

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216 and healthcare professionals see this as a feasible method for diabetes prevention [40]. However,
217 the potential for patients to be health messengers in their families may be dependent on culture.
218 Previous research shows that people from certain cultural backgrounds may be more likely to
219 discuss familial risk of type 2 diabetes with their relatives [39, 41, 42]. For example, Surinamese
220 patients expressed more concern about their relatives' risk of diabetes, compared to Dutch patients
221 [41]. Another study showed that people from Bahrain are less likely to take responsibility to prevent
222 type 2 diabetes and to be influenced by medical advice in comparison to people from Ireland [42].

223 Only one study in this review used communication of familial risk of type 2 diabetes directly to
224 relatives as a tool for behavior change [23] and showed significant changes in some of the primary
225 outcomes. Previous research indicates that informing people about their familial risk increases
226 people's feelings of control over their ability to prevent type 2 diabetes [43], and their perception of
227 personal risk [44], suggesting that such interventions are potentially simpler and cheaper, and
228 require further investigation. One study delivered the intervention online by emailing participants
229 tailored lifestyle recommendations (27). Although the study did not find significant long-term
230 changes in primary outcomes, it represents an early step in the use of online interventions. A more
231 recent study showed that an interactive web-based intervention can have a significant impact on
232 physical activity and dietary intake for people with a metabolic syndrome [45]. Computerized, online
233 interventions have the potential to reach a large number of people at high risk of type 2 diabetes
234 and provide personalized feedback and ongoing support to further support sustained behavior
235 change.

236 The majority of studies in this review demonstrated intervention effectiveness. The use of
237 established behavior change techniques varied, ranging from two to 12 but there was no clear link
238 between number of behavior change techniques and intervention effectiveness. In addition, three of
239 the studies were at high risk of bias in one [22], two [24-26] or three [27] of the domains of the

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240 Cochrane Collaboration's tool [21]. A combination of diet and exercise education appeared to lead
241 to most significant changes in weight loss [15-18, 22]. However, such interventions are very costly.
242 Moreover, only two studies reported sustained behavior change at two years follow-up [15-18, 22],
243 raising concern over long-term sustainability.

244 This review also raises questions as to the practicality of recruiting people who are at high risk of
245 type 2 diabetes by virtue of having a relative with diabetes. The potential of behavior change studies
246 among relatives would be undermined if recruitment of participants is not successful. However, the
247 most effective recruitment strategies remain unclear. Although the studies in this review report on
248 their recruitment methods, they do not provide detailed information about the effectiveness of
249 these methods. The yield of eligible people was very low when they were recruited via relatives who
250 were taking part in larger RCTs [14, 28-30], although by definition this strategy is not translatable to
251 the real world context. The proportions of eligible people who were recruited when they were
252 identified through their own health care contacts was much higher and this could be a more
253 promising approach for targeting them. However, the number of people who need to be screened in
254 order to identify eligible people may be very high. In addition, systematic screening of family
255 members of people with type 2 diabetes is unlikely for logistic and financial reasons, which further
256 strengthens the argument for the potential of patients to act as health educators within their
257 families.

258 To conclude, this review has identified two main challenges that need to be addressed in order to
259 optimize diabetes prevention in high-risk relatives and partners of people with type 2 diabetes: the
260 development of effective interventions that are sustainable and not demanding on participants' time
261 and cost; and simple and feasible methods of recruiting people who would benefit most from them.

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264

265 **References**

266 [1] M. Pierce, H. Keen, C. Bradley. Risk of diabetes in offspring of parents with insulin-dependent
267 diabetes, *Diabet Med* 12 (1995) 6-13.

268 [2] C. Weijnen, S. Rich, J. Meigs, A. Krolewski, J. Warram. Risk of diabetes in siblings of index cases
269 with type 2 diabetes: Implications for genetic studies, *Diabet Med* 19 (2002) 41-50.

270 [3] R. Valdez. Detecting undiagnosed type 2 diabetes: Family history as a risk factor and screening
271 tool, *J Diabetes Sci Technol* 3 (2009) 722-726.

272 [4] A. Weinstein Relationship of physical activity vs body mass index with type 2 diabetes in women,
273 *JAMA* 292 (2004) 1188-1194.

274 [5] J. Sun, J. Lu, W. Wang, Y. Mu, J. Zhao, C. Liu, L. Chen et al. Prevalence of Diabetes and
275 Cardiometabolic Disorders in Spouses of Diabetic Individuals, *Am J Epidemiol* 184 (2016) 400-409.

276 [6] A. Kirk, N. Mutrie, P. MacIntyre, M. Fisher. Increasing physical activity in people with type 2
277 diabetes, *Diabetes Care* 26 (2003) 1186-1192.

278 [7] S. Klein, N. Sheard, X. Pi-Sunyer, A. Daly, J. Wyllie-Rosett. Weight management through lifestyle
279 modification for the prevention and management of type 2 diabetes: Rationale and strategies,
280 *Diabetes Care* 27 (2004) 2067-2073.

281 [8] C. Di Loreto, C. Fanelli, P. Lucidi, F. Murdolo, A. De Cicco. Make your diabetic patients walk: long-
282 term impact of different amounts of physical activity on type 2 diabetes, *Diabetes Care* 28 (2005)
283 1295-1302.

Interventions for prevention of type 2 diabetes in relatives: A systematic review

- 284 [9] C. Gillies, K. Abrams, P. Lambert, N. Cooper, A. Sutton. Pharmacological and lifestyle interventions
285 to prevent or delay type 2 diabetes in people with impaired glucose tolerance: Systematic review
286 and meta-analysis, *BMJ* 334 (2007) 299.
- 287 [10] J. Gill, A. Cooper. Physical activity and prevention of type 2 diabetes mellitus. *Sports Med* 38
288 (2008) 807-824.
- 289 [11] T. Harrison, H. Kim, R. Wines, D. Bowen, B. McGrath. Family history of diabetes as a potential
290 public health tool, *Am J Prev Med* 24 (2003) 152-159.
- 291 [12] W. Heideman, B. Middelkoop, V. Nierkens, K. Stronks, A. Verhoeff, S. van Esch. Changing the
292 odds. What do we learn from prevention studies targeted at people with a positive family history of
293 type 2 diabetes, *Prim Care Diabetes* 5 (2011) 215-221.
- 294 [13] B. Iraj, N. Taheri, M. Amini, P. Amini, A. Aminorroaya. Should the first degree relatives of type 2
295 diabetes patients with isolated impaired fasting glucose be considered for a diabetes primary
296 prevention program? *J Res Med Sci* 15 (2010) 264-269.
- 297 [14] A. Gorin, R. Wing, J. Fava, J. Jakicic, R. Jeffery. Weight loss treatment influences untreated
298 spouses and the home environment: evidence of a ripple effect, *Int J Obes* 32 (2008) 1678-1684.
- 299 [15] H. Brekke, P. Jansson, J. Mansson, R. Lenner. Lifestyle changes can be achieved through
300 counselling and follow-up in first-degree relatives of patients with type 2 diabetes. *J Am Diet Assoc*
301 103 (2003) 835-843.
- 302 [16] H. Brekke, A. Sunesson, M. Axelsen. Attitudes and barriers to dietary advice aimed at reducing
303 risk of type 2 diabetes in first-degree relatives of patients with type 2 diabetes. *J Hum Nutr Diet* 17
304 (2004) 513-521.
- 305 [17] H. Brekke, R. Lenner, M. Taskinen, J. Mansson, T. Funahashid. Lifestyle modification improves
306 risk factors in type 2 diabetes relatives. *Diabetes Res Clin Pract* 68 (2005) 18-28.

Interventions for prevention of type 2 diabetes in relatives: A systematic review

307 [18] H. Brekke, P. Jansson, R. Lenner. Long-term (1- and 2-year) effects of lifestyle intervention in
308 type 2 diabetes relatives. *Diabetes Res Clin Pract* 70 (2005) 225-234.

309 [19] D. Altman, J. Bland. Treatment allocation by minimisation. *BMJ* 330 (2005) 843.

310 [20] C. Abraham, S. Michie. A Taxonomy of Behavior Change Techniques Used in Interventions.
311 *Health Psychol* 27 (2008) 379-387.

312 [21] J. Higgins, D. Altman, P. Gotzsche, P. Juni, D. Moher. The Cochrane Collaboration's tool for
313 assessing risk of bias in randomised trials, *BMJ* 343 (2011) d5928.

314 [22] R. Wing, E. Venditti, J. Jakicic, B. Polley, W. Lang. Lifestyle intervention in overweight individuals
315 with a family history of diabetes, *Diabetes Care* 21 (1998) 350-359.

316 [23] M. Pijl, D. Timmermans, L. Claasen, J. Janssens, G. Nijpels Impact of communicating familial risk
317 of diabetes on illness perceptions and self-reported behavioral outcomes, *Diabetes Care* 32 (2009)
318 597-599.

319 [24] W. Heideman, V. Nierkens, K. Stronks, B. Middelkoop, J. Twisk. DiAlert: a lifestyle education
320 programme aimed at people with a positive family history of type 2 diabetes and overweight, study
321 protocol of a randomised controlled trial, *BMC Public Health* 11 (2011) 751.

322 [25] W. Heideman, M. de Wit, B. Middelkoop, V. Nierkens, K. Stronks. DiAlert: a prevention program
323 for overweight first-degree relatives of type 2 diabetes patients: results of a pilot study to test
324 feasibility and acceptability, *Trials* 13 (2012) 178.

325 [26] W. Heideman, M. de Wit, B. Middelkoop, V. Nierkens, K. Stronks. Diabetes risk reduction in
326 overweight first-degree relatives of type 2 diabetes patients: effects of a low-intensive lifestyle
327 education program (DiAlert) A randomized controlled trial, *Patient Educ Couns* 98 (2015) 476-483.

Interventions for prevention of type 2 diabetes in relatives: A systematic review

- 328 [27] Y. Tokunaga-Nakawatase, M. Nishigaki, C. Taru, I. Miyawaki, J. Nishida. Computer- supported
329 indirect-form lifestyle modification support program using Lifestyle Intervention Support Software
330 for diabetes prevention (LISS-DP) for people with a family history of type 2 diabetes in a medical
331 check up setting, *Prim Care Diabetes* 8 (2014) 208-214.
- 332 [28] K. Williams, T. Prevost, S. Griffin, W. Hardeman, W. Hollingworth. The ProActive trial protocol - a
333 randomised controlled trial of the efficacy of a family-based, domicillary intervention programme to
334 increase physical activity among individuals at high risk of diabetes [ISRCTN61323766], *BMC Public
335 Health* 4 (2004) 48.
- 336 [29] A. Kinmonth, N. Wareham, W. Hardeman, S. Sutton, T. Prevost. Efficacy of a theory-based
337 behavioural intervention to increase physical activity in an at-risk group in primary care (ProActive
338 UK): a randomised trial, *Lancet* 371 (2008) 41-48.
- 339 [30] W. Hardeman, A. Kinmonth, S. Michie, S. Sutton, T. Prevost. Impact of a physical activity
340 intervention program on cognitive predictors of behaviour among adults at risk of type 2 diabetes
341 (ProActive randomised controlled trial). *Int J Behav Nutr Phys Act* 6 (2009).
- 342 [31] A. Spijkerman, C. Stehouwer, M. Adriaanse, L. Bouter, J. Dekker, R. Heine, G. Nijpels. Diabetic
343 Patients Detected by Population-Based Stepwise Screening Already Have a Diabetic Cardiovascular
344 Risk Profile, *Diabetes Care* 25 (2002) 1784-1789.
- 345 [32] G. Bodenmann, N. Meuwly, K. Kayser. Two conceptualizations of dyadic coping and their
346 potential for predicting relationship quality and individual well-being: a comparison, *Europ Psych* 16
347 (2011) 255-266.
- 348 [33] R. Lyons, K. Mickelson, M. Sullivan, J. Coyne. Coping as a communal process. *J Soc Pers Relat* 15
349 (1998) 579-605.

Interventions for prevention of type 2 diabetes in relatives: A systematic review

- 350 [34] M. Crossno. Bowen Family Systems Theory. In L. Metcalf. Marriage and Family Therapy: A
351 practice-oriented approach, Springer Publishing Company, New York (2011) 39-65.
- 352 [35] W. Demark-Wahnefried, L. Jones, D. Snyder, R. Sloane, G. Kimmick, D. Hughes et al. Daughters
353 and mothers against breast cancer (DAMES): Main outcomes of a randomized controlled trial of
354 weight loss in overweight mothers with breast cancer and their overweight daughters. *Cancer* 120
355 (2014) 2522-2534.
- 356 [36] S. van Esch, M. Nijkamp, M. Cornel, G. Snoek. Patients' intentions to inform relatives about Type
357 2 diabetes risk: the role of worry in the process of family risk disclosure. *Diabet Med* 29 (2012) e461-
358 e467.
- 359 [37] D. Whitford, H. McGee, B. O'Sullivan. Will people with type 2 diabetes speak to family members
360 about health risk? *Diabetes Care* 32 (2009) 251-253.
- 361 [38] S. van Esch, M. Nijkamp, M. Cornel, F. Snoek. Illness representations of type 2 diabetes patients
362 are associated with perceptions of diabetes threat in relatives. *J Health Psychol* 19 (2014) 358-368.
- 363 [39] D Whitford, H. McGee, B. O'Sullivan. Reducing health risk in family members of patients with
364 type 2 diabetes: views of first degree relatives. *BMC Public Health* 9 (2009) 455.
- 365 [40] S. van Esch, W. Heideman, W Cleijne, M. Cornel, F. Snoek. Health care providers' perspective on
366 using family history in the prevention of type 2 diabetes: a qualitative study including different
367 disciplines. *BMC Fam Practice* 14 (2013).
- 368 [41] S. van Esch, M. Cornel, P. Geelhoed-Duijvestijn, F. Snoek. Family communication as strategy in
369 diabetes prevention: An observational study in families with Dutch and Surinamese South-Asian
370 ancestry. *Patient Educ Couns* 87 (2012) 23-29.
- 371 [42] D. Whitford, M. Al-Sabbagh. Cultural variations in attitudes towards family risk of diabetes.
372 *Diabetes Res Clin Prac* 90 (2010) 173-181.

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373 [43] M. Nishigaki, Y. Tokunaga-Nakawatase, J. Nishida, K. Kazuma. The effect of genetic counseling
374 for adult offspring of patients with type 2 diabetes on attitudes toward diabetes and its heredity: a
375 randomized controlled trial. *J Gen Couns* 23 (2014) 762-769.

376 [44] M. Pierce, D. Ridout, D. Harding, H. Keen, C. Bradley. More good than harm: a randomised
377 controlled trial of the effect of education about familial risk of diabetes on psychological outcomes,
378 *Brit J Gen Pract* 50 (2000) 867-871.

379 [45] L. Jahangiry, A. Montazeri, M. Najafi, M. Yaseri, M. Farhangi. An interactive web-based
380 intervention on nutritional status, physical activity and health-related quality of life in patient with
381 metabolic syndrome: a randomized-controlled trial (The Red Ruby Study). *Nutr & Diabetes* 7 (2017)
382 e240.

383 [46] D. Moher, A. Liberati, J. Tetzlaff, D. Altman, The PRISMA Group. Preferred Reporting Items for
384 Systematic Reviews and Meta-Analyses: The PRISMA Statement, *PLoS Med* 6 (2009) e1000097.

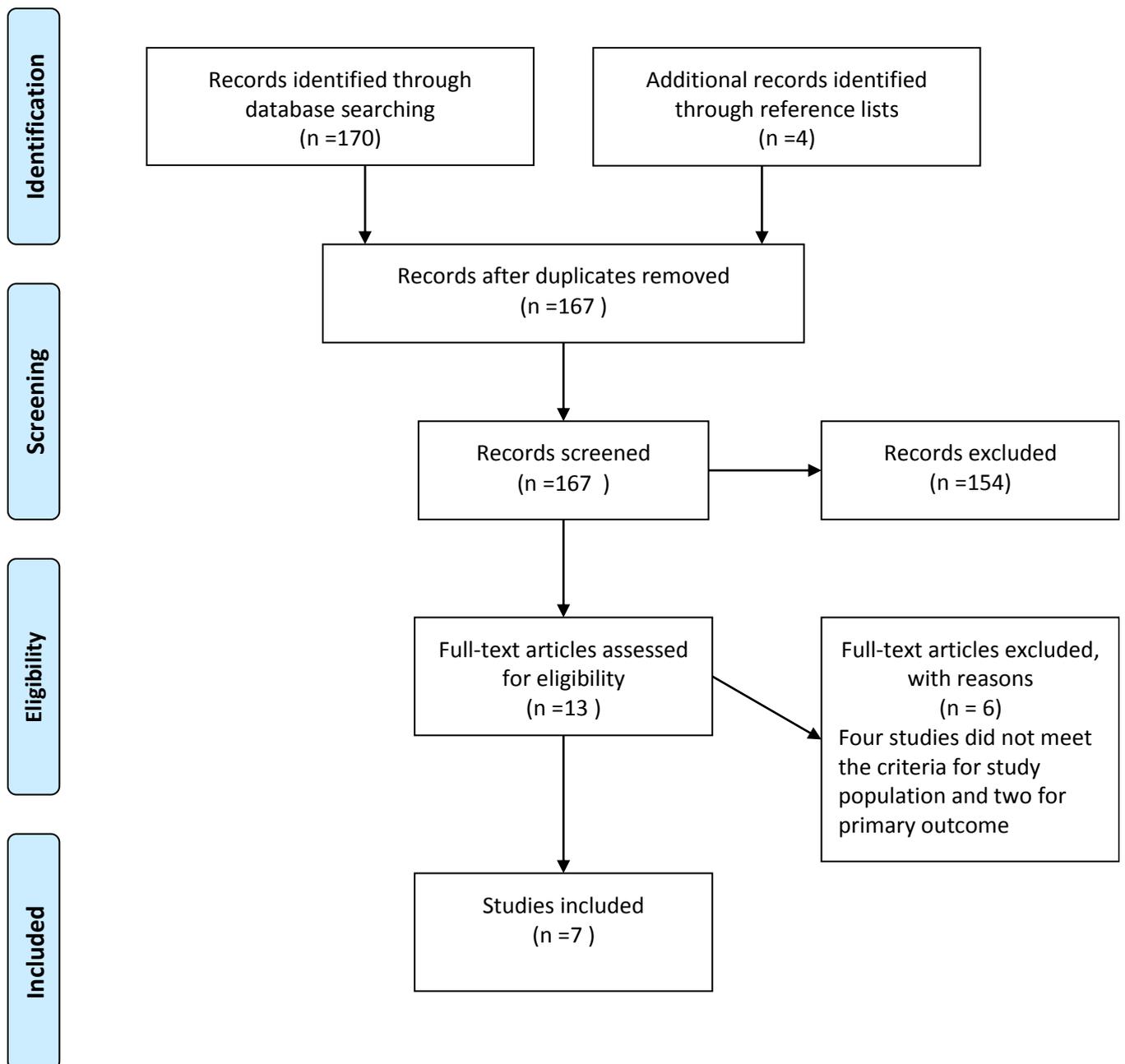
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386 Figure 1 Identification and selection of studies (Adapted from Moher, Liberati, Tetzlaff, Altman & The

387 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Group [46]).

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Table 1. Summary of included studies

	Population sample	Recruitment methods	Intervention components and mode of delivery	Intervention duration	Study outcomes	Behaviour change techniques
Wing et al., 1998 (USA) [22]	<p>Offspring</p> <p>Age: M=45.7 yrs BMI: M=35.9 kg/m² Gender: 79% women Education: not reported Occupation: not reported Ethnicity: not reported</p>	<p>Newspaper adverts for overweight people aged 40-55 yrs with a parent with diabetes</p> <p>N = 154</p>	<p>3 interventions groups, 1 control.</p> <p>Diet group: Behavioral strategies to modify food intake, such as provision of plans and goals and self-monitoring</p> <p>Exercise group: A lecture on changing exercise behavior and a 50-60 minute walk with an exercise therapist plus a second supervised walk every week for the first 10 weeks of the study.</p> <p>Diet + Exercise group: A combination of components from diet and exercise groups</p> <p>Control group: A manual on healthy eating and exercise.</p>	<p>2 years: weekly meetings for 6 months followed by biweekly meetings for another 6 months. Two courses in 2nd year.</p>	<p>Body weight; daily calorie intake, physical activity.</p> <p>Most significant changes in weight loss and physical activity at 2-year follow up in diet plus exercise group.</p> <p>Weight loss led to a reduction of risk of type 2 diabetes with 31%.</p> <p>Sustained decrease in calorie intake in the diet group.</p>	<p>T4: Prompt intention formation T5: Prompt barrier identification T7: Set graded tasks T8: Provide instruction T9: Model or demonstrate the behavior T10: Prompt specific goal setting T11: Prompt review of behavioral goals T12: Prompt self-monitoring of behavior T13: Provide feedback on performance T17: Prompt practice T18: Use follow-up prompts T23: Relapse prevention</p>
Brekke et al., 2003 (Sweden) [15-18]	<p>First-degree relatives</p> <p>Age: M=42.4yrs BMI: M=25.8 kg/m² Gender: 36.1% women Education: not reported</p>	<p>Patients at diabetes clinic completed questionnaire about diabetes in family members. Letter or phone call to those with non-diabetic relatives - asked to contact them.</p>	<p>2 intervention groups, 1 control</p> <p>Diet group: Diet advice and goal setting</p> <p>Diet + exercise group: Diet advice and discussion about physical activity</p> <p>Control: A letter with advice to maintain current lifestyle</p>	<p>Two sessions and phone calls every 10 days for 4 months</p>	<p>Body weight; waist circumference; sagittal diameter; energy intake; physical activity; diet adherence.</p> <p>Significant decrease in body weight, waist circumference and sagittal</p>	<p>T2: Provide information on consequences T4: Prompt intention formation T8: Provide instruction T10: Prompt specific goal setting T12: Prompt self-monitoring of behavior</p>

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	Occupation: not reported Ethnicity: not reported	Newspaper adverts N = 77			diameter in the diet plus exercise group. Significant changes in diet adherence for both intervention groups at 1- and 2-year follow-up. Weight loss was sustained in the diet plus exercise group at 2-year follow-up. No significant changes in physical activity.	T13: Provide feedback on performance T18: Use follow-up prompts
Gorin et al., 2008 (USA) [14]	Partners Age: M=59.2 yrs BMI: M=30.6 kg/m ² Gender: 57% women Education: 68.3% attending college or more Occupation: not reported Ethnicity:91.5% Caucasian	Among 5,145 overweight people with type 2 diabetes in LookAHEAD RCT in 16 centers, there were 607 married or living with significant other, 357 partners agreed to take part N=357	1 intervention, 1 control group Intervention group: Combination of group and individual meetings; training in self-monitoring, problem solving, goal setting, relapse prevention and enhancing social support; information on controlling physical cues (e.g. storing food out of sight) and social cues (e.g. avoid temptation. Control group: Enhanced usual care-three information group meetings per year that provided information on diabetes, nutrition and physical activity.	Four meetings per month for 6 months followed by 3 sessions per month for another 6 months.	Body weight; energy intake; behavioral control strategies; physical activity. Partners of intervention participants were more likely to adopt strategies for behavior control and lost significantly more weight and reduced energy intake at 1-year follow-up, compared to partners of control group participants. No significant changes in physical activity.	T5: Prompt barrier identification T10: Prompt specific goal setting T12: Prompt self-monitoring of behavior T20: Plan social support or social change T23: Relapse prevention

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<p>Proactive trial, 2004 (UK) [28-30]</p>	<p>(Sedentary) offspring Age: M=40.4 yrs BMI: M=27.8 kg/m² Gender: 62% women Education: Mean age when they finished education- 17.9 Occupation: 55.3% in managerial or professional job Other SES information: 89% owned a home; 98% had a car Ethnicity: Predominantly white</p>	<p>1,521 potentially eligible offspring of people with type 2 diabetes were recruited by searching primary care records and sent questionnaire. 1,123 were returned and 465 eligible people contacted. 399 agreed to take part. 365 were randomized. N = 365</p>	<p>2 intervention groups, 1 control Intervention groups: Individual lifestyle intervention over the phone or in person; behavioral strategies such as goal setting, action planning, self-monitoring and building support from family and friends. Control group: An advice leaflet</p>	<p>Phone intervention: 6 phone calls over 5 months then monthly postal contact for 7 months. Home intervention: 4 visits and 2 phone calls for 5 months then monthly phone calls for 7 months</p>	<p>Body weight; BMI; waist circumference; blood pressure; cholesterol; physical activity. No significant changes in study outcomes.</p>	<p>T2: Provide information on consequences T4: Prompt intention formation T7: Set graded tasks T10: Prompt specific goal setting T11: Prompt review of behavioral goals T12: Prompt self-monitoring of behavior T15: Teach to use prompts or cues T18: Use follow-up prompts T20: Plan social support or social change T23: Relapse prevention</p>
<p>Pijl et al., 2009 (The Netherlands) [23]</p>	<p>First-degree relatives Age: M=67.1 yrs BMI: M=28.3 kg/m² Gender: 57% women Education: 5% completed higher</p>	<p>233 participants of a diabetes screening program 5 years previously who had family history invited to RCT. 118 participated. N = 118</p>	<p>1 intervention, 1 control group Intervention group: Communication of genetic risk by constructing a family tree; discussion on familial risk and information on prevention. Control group: A five-year risk estimate, based on general risk factors.</p>	<p>One session</p>	<p>Healthy eating; physical activity; behavioral intentions. Significant increase in healthy eating in the intervention group.</p>	<p>T1: Provide information about behavior-health link T2: Provide information on consequences</p>

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	vocational training Occupation: not reported Ethnicity: Dutch Caucasian				Marginally significant changes in physical activity between groups. No change in behavioral intentions.	
Heideman et al., 2011 (The Netherlands) [24-26]	Parents and/or siblings Age: M=55 yrs BMI: M=30.5 kg/m ² Gender: 67.7% women Education: 49.5% low, 18.9% middle, 31.6% high Occupation: not reported Ethnicity: 80% Dutch, 4.2% Surinamese, 4.2% Netherlands East Indies, 2.1% Antilles	Letter from GP to potentially eligible people from primary care records. Adverts in community. Women from gestational diabetes clinics. N = 482	1 intervention, 1 control group Intervention group: Discussion about risk factors for type 2 diabetes, health benefits of lifestyle changes, self-monitoring and physical activity diaries; nutrition and exercise balance, benefits and barriers of lifestyle change and setting personal action plans; newsletters about healthy eating and physical activity. Control group: A brochure about heredity and general risk factors for type 2 diabetes.	Two sessions over a 2 week period	Waist circumference; blood pressure; intention to change; diet; physical activity; smoking; alcohol intake. Sustained decrease in waist circumference and improved systolic blood pressure in the intervention group. No significant changes in intention to change, diet, physical activity, smoking or alcohol intake.	T1: Provide information about behavior-health link T2: Provide information on consequences T4: Prompt intention T5: Prompt barrier identification T10: Prompt specific goal setting T12: Prompt self-monitoring of behavior T17: Prompt practice T23: Relapse prevention
Tokunaga-Nakawata se et al., 2012 (Japan) [27]	Parents and/or siblings Age: M=44.9 yrs BMI: M=22.7 kg/m ² Gender: 67.1% men	Recruited at a medical check-up. 216/538 eligible individuals consented to be randomized. 141 were enrolled. N = 141	1 intervention, 1 control group Intervention group: Tailored, concrete lifestyle recommendations via email in addition to a pamphlet about general diabetes prevention.	Three emails over 6 months	Energy intake; physical activity; biomedical factors. Intervention effectiveness for all primary outcomes was observed during the	T1: Provide information about behavior-health link T2: Provide information on consequences T8: Provide instruction

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	<p>Education: 3 less than high school, 28 high school, 29 technical school, 75 university/college, 6 graduate school Occupation: 122 full-time, 16 part-time, 2 housekeeping Ethnicity: not reported</p>		<p>Control group: The same pamphlet and conventional routine care.</p> <p>Individual lifestyle intervention via email and a pamphlet</p>		<p>intervention but not thereafter.</p>	
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Table 2 Risk of bias assessments of included studies

	Random sequence generation.	Allocation concealment.	Blinding of participants and personnel.	Blinding of outcome assessment.	Incomplete outcome data.	Selective reporting.	Other sources of bias.
Wing et al., 1998	L	U	L	L	U	L	H ¹
Brekke et al., 2003	L	U	U	U	L	L	L
Gorin et al., 2008	L	L	U	L	U	L	L
Proactive trial, 2004	L	L	U	L	L	L	L
Pijl et al., 2009	L	L	U	U	L	L	L
Tokunaga - Nakawata se et al., 2012	L	L	H	L	H	H	L
Heideman et al., 2011	L	L	H	L	L	L	H ²

1. High risk of other bias because there was a significant difference in session attendance between groups.
2. High risk of other bias because Study was underpowered; anthropometric measurements were not blinded to treatment allocation; intervention fidelity was not objectively measured.

