

Lifestyle Interventions Are Cost-Effective in People With Different Levels of Diabetes Risk

Results from a modeling study

MONIQUE A.M. JACOBS-VAN DER BRUGGEN,
MSC
GRIËT BOS, PHD
WANDA J. BEMELMANS, PHD

RUDOLF T. HOOGENVEEN, MSC
SYLVIA M. VIJGEN, MSC
CAROLINE A. BAAN, PHD

OBJECTIVE — In the current study we explore the long-term health benefits and cost-effectiveness of both a community-based lifestyle program for the general population (community intervention) and an intensive lifestyle intervention for obese adults, implemented in a health care setting (health care intervention).

RESEARCH DESIGN AND METHODS — Short-term intervention effects on BMI and physical activity were estimated from the international literature. The National Institute for Public Health and the Environment Chronic Diseases Model was used to project lifetime health effects and effects on health care costs for minimum and maximum estimates of short-term intervention effects. Cost-effectiveness was evaluated from a health care perspective and included intervention costs and related and unrelated medical costs. Effects and costs were discounted at 1.5 and 4.0% annually.

RESULTS — One new case of diabetes per 20 years was prevented for every 7–30 participants in the health care intervention and for every 300–1,500 adults in the community intervention. Intervention costs needed to prevent one new case of diabetes (per 20 years) were lower for the community intervention (€2,000–9,000) than for the health care intervention (€5,000–21,000). The cost-effectiveness ratios were €3,100–3,900 per quality-adjusted life-year (QALY) for the community intervention and €3,900–5,500 per QALY for the health care intervention.

CONCLUSIONS — Health care interventions for high-risk groups and community-based lifestyle interventions targeted to the general population (low risk) are both cost-effective ways of curbing the growing burden of diabetes.

Diabetes Care 30:128–134, 2007

Risk factors for developing type 2 diabetes include a high body weight, physical inactivity, and smoking, whereas moderate consumption of alcohol or coffee appears to be protective (1–9). The most serious of these factors is overweight. With every 1 unit increase in BMI, the risk of developing type 2 diabe-

tes increases by ~10–30% (10). There is substantial evidence that lifestyle interventions focused on diet and physical exercise can reduce diabetes incidence in individuals at high risk of developing diabetes (11–14). Although the direct effect of lifestyle interventions on diabetes incidence in other target populations is rela-

tively unknown, it is suggested that a relatively small shift of the entire general population toward more healthy behavior could lead to a reduction in the incidence of diabetes (15).

Modeling can be used to assess the potential long-term impact of lifestyle programs on future health and health care costs. Such information is interesting to policy makers who have to decide on optimal allocation of limited budgets. Models have been used to demonstrate that intensive lifestyle modification programs are cost-effective for individuals at high risk of developing diabetes (16,17). However, the cost-effectiveness of such interventions for individuals at lower risk of developing diabetes is relatively unknown (15,16,18–20). The incidence of diabetes in individuals without a high risk of developing this disease has been assessed directly in only a few lifestyle intervention studies (18,21). However, effects on the most important diabetes risk factors, BMI and physical inactivity, have been evaluated for different kinds of lifestyle interventions in different target populations. The long-term impact of lifestyle interventions can be modeled through modifying risk factor levels, with the advantage that effects of risk factor modification on all-cause mortality and diseases other than type 2 diabetes can be taken into account (22).

Therefore, the aim of this study was to explore and compare the cost-effectiveness of lifestyle interventions for individuals at different levels of diabetes risk, using the National Institute for Public Health and the Environment (RIVM) chronic diseases model (CDM). The CDM is a Markov type, dynamic population model that describes transitions between risk factors, chronic diseases, and mortality (23). This allows the effects of risk factor modification on mortality and the incidence and prevalence of several diseases to be measured. A second aim was to explore the potential health benefits for large-scale implementation of lifestyle interventions in the Netherlands.

From the National Institute for Public Health and the Environment, Bilthoven, the Netherlands.

Address correspondence and reprint requests to Monique A.M. Jacobs-van der Bruggen, National Institute for Public Health and the Environment, Department of Prevention and Health Services Research, P.O. Box 1, 3720 BA, Bilthoven, Netherlands. E-mail: monique.jacobs@rivm.nl.

Received for publication 30 March 2006 and accepted in revised form 1 October 2006.

Additional information for this article can be found in an online appendix at <http://care.diabetesjournals.org>.

Abbreviations: CDM, chronic diseases model; DPP, Diabetes Prevention Program; NNT, number needed to treat; QALY, quality-adjusted life-year; RIVM, National Institute for Public Health and the Environment.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-0690

© 2007 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

RESEARCH DESIGN AND METHODS

A large amount of data are available about the long-term effects of two types of interventions, namely, community-based lifestyle programs and intensive lifestyle programs for high-risk groups (24–27). Typically, community programs comprise mass media campaigns and a range of activities in various settings with the aim of changing risk factor behavior in the general population. Lifestyle interventions for high-risk groups are typically implemented in a health care setting and comprise dietary advice, exercise programs, and/or behavior modification therapy for individuals or groups. In the current study, we explore the lifetime health effects and cost-effectiveness of a once-only implementation of the following interventions: 1) a community-based program with a duration of 5 years, focusing on nutrition and exercise and targeted to the general population, referred to as “community intervention,” and 2) an intensive lifestyle intervention with a duration of 3 years, focusing on diet and exercise, for adults with moderate risks of developing diabetes (obese adults 30–70 years), implemented in a health care setting, referred to as “health care intervention.”

Short-term effects on BMI and physical (in)activity are estimated from published studies, which are representative for the aforementioned interventions. In general, community programs have modest effects on body weight and physical inactivity (25,28–32), whereas, on average, the effects of health care interventions are larger (11–13,26,33). In the current study, potential intervention effects are expressed within a range that reflects the diversity of positive intervention effects that we found in the international literature.

Effects of the community intervention are defined as minimum effect, average BMI decreases by 0.05 kg/m² and physical (in)activity is unchanged, and maximum effect, average BMI decreases by 0.25 kg/m² and 15% of inactive individuals increase their level of physical activity (to moderately active). Effects are assumed for adults 20–80 years of age.

Effects of the health care intervention are defined as minimum effect, average BMI decreases by 0.3 kg/m² and 50% of inactive individuals increase their level of physical activity (to moderately active), and maximum effect, average BMI decreases by 1.5 kg/m², 75% of inactive in-

dividuals become moderately active, and 20% of moderately active individuals increase their level of physical activity (to active).

In the current study, intervention costs are based on two Dutch projects. The community-based program, Hartslag Limburg (Heart Health Limburg), is aimed to decrease the prevalence of cardiovascular diseases in the general population (34). Total intervention costs for activities focusing on nutrition and physical activity for 5 years were ~€4.50 per inhabitant (or €6 per adult ≥20 years of age) in the target area (35). The Study on Lifestyle Intervention and Impaired Glucose Tolerance Maastricht is an intensive lifestyle intervention with the aim of improving lifestyle in overweight subjects with impaired glucose tolerance by means of a 3-year dietary advice program and an exercise program (36,37). The cost calculations for this intervention are briefly outlined in online Appendix A (available at <http://care.diabetesjournals.org>). The costs for large-scale implementation are estimated to be ~€700 per participant, based on the assumption that 50% of the participants will participate in the exercise program. Health effects, intervention costs, and effects on health care costs are assumed to be proportional to the number of intervention participants (which implies that the cost-effectiveness ratios are independent on the reach of the interventions).

For each intervention, the CDM computes lifetime health effects, effects on health care costs, and costs per quality-adjusted life-year (QALY) resulting from the minimum and maximum estimated intervention effect. In the model, each intervention is compared with a reference scenario that describes developments in the Dutch population when no interventions are applied.

The RIVM CDM

The CDM is a Markov-type, multistate transition model, developed at RIVM (38–42). An extensive description of the CDM structure and the relevant input data used are given in online Appendix B (available at <http://care.diabetesjournals.org>). The model was updated for diabetes in 2005 (43). In short, the model describes the development over time of demography, risk factor prevalence, disease incidence, and mortality in the Dutch population. In the CDM, BMI and physical activity are each modeled in three classes: for BMI, normal weight (BMI <25 kg/m², class 1), overweight (BMI 25–30

kg/m², class 2), and obesity (BMI ≥30 kg/m², class 3); and for physical activity, active (30 min of activity of moderate intensity on at least 5 days/week, class 1), moderately active (30 min of activity of moderate intensity on 1–4 days/week, class 2), and inactive (30 min of activity of moderate intensity on <1 day/week, class 3). BMI and physical activity are linked to all-cause mortality, diabetes, cardiovascular diseases, musculoskeletal disorders, and cancers through relative risks on disease incidence (43,44). Relative risks are based on the international literature, whereas incidence, prevalence, transition rates, and mortality rates in the model apply to the Dutch population. All data are age and sex specific. Health care costs are based on the Costs of Illness study in the Netherlands (45,46). The Global and Dutch Burden of Disease studies are used to compute health effects in terms of QALYs (46–50). Recently, the RIVM model was extended with a module for cost-effectiveness analyses (46).

The cohort in the start year of the simulation resembled the total Dutch population at the end of 2004 ($n = 16.3$ million). Newborns or migrants are not included in the analysis. The time step used for modeling is 1 year. A lifetime horizon (70 years) is applied.

Translation of intervention effects into model parameters

The intervention effects on BMI and physical activity were translated into altered prevalence rates in each risk factor class in the model. For example, we assumed that all adults in the Netherlands had been reached by the community intervention. At the end of year 5, the prevalence of normal weight (BMI class 1) in the community scenario (maximum effect) was 2.4% points higher than that in the reference scenario (52.4 vs. 50%). The differences in BMI classes 1–3 and physical activity classes 1–3 (in percentage points) were +2.4, –1.1, –1.3, no change, +1.2, and –1.2, respectively. For the health care intervention, we assumed that 200,000 obese adults participated. In the maximum-effect scenario, differences between the intervention and reference scenario after 3 years in BMI classes 1–3 and physical activity classes 1–3 (in percentage points) were no change, +1.7, –1.7, +0.2, +0.1, and –0.3, respectively. After the interventions, yearly age- and sex-specific transition probabilities between risk factor classes (e.g., the chance to gain weight with aging) were equal for the in-

Table 1—Effects on health, health care costs, and cost-effectiveness of lifestyle interventions

Outcome	Community intervention	Health care intervention
Health effects		
Life years*	0.007–0.043 2–16 days	0.32–1.35 4–16 months
QALYs*	0.006–0.039 2–15 days	0.27–1.17 3–14 months
NNT to prevent 1 case of diabetes in 20 years	1,500–300	30–7
NNT to prevent 1 case of cardiovascular disease in 20 years	3,700–400	60–18
Costs†		
Intervention costs	5.55	675
Δlifetime related medical costs	–10 to –70	–500 to –1,700
Δlifetime unrelated medical costs	30–180	1,300–5,600
Δlifetime total medical costs	20–110	800–3,900
Cost-effectiveness		
Intervention costs per QALY	900–140	2,500–600
Related costs per QALY‡	–500 to –1,500	800 to –900
Total costs per QALY§	3,900–3,100	5,500–3,900

All ranges correspond to result when “minimum intervention effect” is assumed to result when a “maximum intervention effect” is assumed. *Effect per intervention participant; life-years and QALYs are discounted by 1.5%/year. †Costs per adult or intervention participant in 2005 in euros, discounted by 4%/year. ‡Intervention costs and lifetime related medical costs. §Intervention costs and lifetime total medical costs.

intervention and reference scenarios. As a result of extinction of the intervention cohorts, the differences between intervention and reference scenarios gradually declined to zero.

Cost-effectiveness analysis

The cost-effectiveness analysis was performed from a health care perspective, meaning that only health-related effects and costs incurred by the health care system were included. A distinction was made between related and unrelated medical costs (46). Related medical costs are intervention costs and (prevented) medical costs for diseases linked to BMI or physical activity within the CDM. Unrelated medical costs are costs for illnesses, for example, dementia, that may develop in life years gained as a result of the intervention. Costs and effects were discounted by 4 and 1.5%/year according to recent Dutch guidelines (51). A cost-effectiveness ratio of <€20,000 per QALY gained was considered cost-effective (52,53).

Outcome measures

Intervention effects in terms of life-years and QALYs per individual were estimated by dividing the total gain in life-years or QALYs resulting from the interventions (minimum and maximum estimate) by the number of assumed intervention par-

ticipants in each intervention (12 million for the community intervention and 200,000 for the health care intervention). The same parameters applied to effects on health care costs per individual. The number needed to treat (NNT) to prevent one new case of diabetes or cardiovascular disease (in 20 years) was calculated by dividing the number of intervention participants by the cumulative number of incident cases prevented in 20 years. Cost-effectiveness ratios were determined for intervention costs per prevented diabetes case (in 20 years), intervention costs per QALY gained (lifetime), related costs per QALY gained (lifetime), and total costs per QALY gained (lifetime).

Sensitivity analysis

Analyses were performed in which intervention costs and discount rates were varied. Costs for the interventions were varied between €4 and €8 per adult for the community intervention and between €400, €1,000, and €2,000 (comparable to the intervention costs found in the Diabetes Prevention Program [DPP]) (54) per participant for the health care intervention. Both costs and effects were discounted by 0 or 4%/year. Discount rates of 3% on both costs and effects were calculated to enhance comparability with a former study (16).

RESULTS

Health effects

Outcomes for both interventions compared with the reference scenario (no intervention) are displayed in Table 1. On average, health benefits per participant are larger for the health care intervention than for the community intervention: 1.17 vs. 0.04 QALYs based on the maximum estimated intervention effects. This result can be interpreted as an average individual gain of 15 days vs. 14 months of living in good health. The NNT is lower for the health care intervention: 7–30 obese adults should participate in a health care intervention to prevent one new case of diabetes in 20 years, and a community program should reach 300–1,500 adults to obtain the same result.

Costs

Both interventions reduce cumulative lifetime medical costs for diabetes, cardiovascular diseases, and other intervention-related diseases (“Related costs per QALY” in Table 1). Unrelated and total medical costs increase because people live longer as a result of the interventions.

For participants in the health care intervention, lifetime-related medical costs per individual may be reduced by up to €1,700. On the other hand, unrelated health care costs increase by €5,600. Average lifetime total health care costs therefore increase by €3,900 for participants in the health care intervention.

Cost-effectiveness

Intervention costs needed to prevent disease are lower for the community intervention: €1,800–9,000 (300–1,500 × €6) to prevent one new case of diabetes in 20 years versus €4,900–21,000 (7–30 × €700) for the health care intervention (intervention costs not discounted). Related costs per QALY in the community intervention are negative because over a patient’s lifetime, savings in related health care costs are larger than initial intervention costs. Whether the high costs of health care intervention are counterbalanced by savings in related health care costs depends on the intervention effect achieved. Cost-effectiveness ratios in which unrelated medical costs are accounted for are €3,100–3,900 per QALY for the community intervention and €3,900–5,500 for the health care intervention.

Table 2—QALYs and cost-effectiveness of both interventions; sensitivity analyses

	QALYs	Related costs (€)/QALY	Total costs (€)/QALY
Community intervention			
Base-case analysis*	0.006–0.04	–500 to –1,500	3,900–3,100
Intervention costs €4 per adult		–800 to –1,600	3,600–3,100
Intervention costs €8 per adult		–200 to –1,500	4,200–3,200
DR 0% costs and effects	0.01–0.06	–1,300 to –2,300	10,000–9,400
DR 3% costs and effects	0.004–0.03	–1,100 to –2,700	7,700–6,500
DR 4% costs and effects	0.003–0.02	–1,000 to –2,800	7,200–5,800
Health care intervention			
Base-case analysis†	0.27–1.17	800 to –900	5,500–3,900
Intervention costs €400 per participants		–200 to –1,100	4,500–3,600
Intervention costs €1,000 per participants		1,900 to –600	6,600–4,100
Intervention costs €2,000 per participants		5,400–200	10,100–4,900
DR 0% costs and effects	0.41–1.75	–300 to –1,300	12,000–11,200
DR 3% costs and effects	0.19–0.82	800 to –1,600	10,000–7,800
DR 4% costs and effects	0.15–0.66	1,500 to –1,600	10,000–6,900

All ranges correspond to result when “minimum intervention effect” is assumed to result when “maximum intervention effect” is assumed. *Intervention costs €6 per adult and discount rates (DRs) 4% for costs and 1.5% for effects. †Intervention costs €700 per participant and discount rates 4% for costs and 1.5% for effects.

Sensitivity analysis

The results of the sensitivity analysis on QALYs and cost-effectiveness ratios are given in Table 2. Discounting health effects by 4% (vs. 1.5% in the base-case analyses) reduces health benefits by ~50%. For both interventions, all cost-effectiveness ratios remain <€20,000 per QALY.

Large-scale implementation in the Netherlands

The Netherlands has ~12 million adults aged 20–80 years and 1 million obese adults aged 30–70 years. Potential effects of large-scale implementation of the lifestyle intervention in the Netherlands are illustrated in Table 3. Theoretically, a community intervention reaching all adults might prevent 2.4% of the new diabetes cases in 20 years. A health care intervention including 200,000 (20%) of the obese adults in the Netherlands may reduce 20-year diabetes incidence by 1.6%, but intervention costs are high.

CONCLUSIONS — By modeling the effect of risk factor modification on long-term disease incidence, mortality, and health care costs, we demonstrated that lifestyle interventions can be cost-effective in individuals with low or mod-

erate risks of developing diabetes. Community-based lifestyle interventions have been conducted with various results (25,31). In general, effects on weight are modest. The largest effect on weight, the maximum effect of the community intervention in our study (–0.25 kg/m²) was based on this, was found in the Stanford Five City Project (28). In this study, after 5 years the weight increase was 0.7 kg less in intervention communities than in control regions. Most community-based programs fail to have substantial effects on physical activity, but the prevalence of physical inactivity may be reduced (29,32). In contrast, effects of health care interventions on mean body weight can be substantial, especially within the 1st year (21). A recent review revealed that a weight loss of 5% can be achieved within 1 year (27). However, the effect tends to decrease at longer term follow-up (11–13,21,26,33,55). After 3 years, as we simulated in our study, the maximum effect is about 4.5 kg (or 1.5 kg/m²) (11,13). With regard to physical activity, intensive programs have been shown to improve maximum oxygen uptake (13), increase time spent on physical activities (11,12), and reduce physical inactivity (12). As intervention effects differ considerably be-

Table 3—Effects of large-scale implementation of lifestyle interventions in the Netherlands

	Reach of the intervention low estimate	Reach of the intervention high estimate
Community intervention		
Adults reached	2.4 million (20)	12 million (100)
Δlife-years	16,000–104,000	81,000–522,000
ΔQALYs	15,000–95,000	76,000–477,000
Prevented diabetes in 20 years	1,600–8,600 (0.1–0.5)	8,000–43,000 (0.4–2.4)
Prevented CVD in 20 years	600–6,200 (0.0–0.1)	3,000–31,000 (0.1–0.7)
Intervention costs €		
Δrelated medical costs (savings)	20–160 million	100–800 million
Δtotal medical costs	40–280 million	200–1,400 million
Health care intervention		
Obese participants	50,000 (5)	200,000 (20)
Δlife-years	16,000–68,000	64,000–271,000
ΔQALYs	14,000–59,000	56,000–234,000
Prevented diabetes in 20 years	1,500–7,000 (0.1–0.4)	6,000–28,000 (0.3–1.6)
Prevented CVD in 20 years	1,000–2,800 (0.0–0.1)	4,000–11,000 (0.1–0.3)
Intervention costs €		
Δrelated medical costs (savings)	20–70 million	100–300 million
Δtotal medical costs	40–200 million	200–800 million

Data are n (%) unless otherwise indicated. All ranges correspond to result when “minimum intervention effect” is assumed to result when “maximum intervention effect” is assumed; discount rates 4% for costs and 1.5% for effects. CVD, cardiovascular disease.

tween studies, we explored the cost-effectiveness for a range of potential intervention effects. Despite methodological differences, average individual health benefits for participants in the health care intervention in our study were in the same order of magnitude as those projected for participants in the DPP (0.19–0.82 QALYs vs. 0.56 in the DPP, all discounted at 3%) (11). The conclusions in both studies were that intensive lifestyle interventions for individuals at increased risk for diabetes are cost-effective.

The literature on cost-effectiveness of interventions with the aim of primary prevention of diabetes is scarce (20). Only one earlier study assessed the cost-effectiveness of a community-based program aimed to prevent diabetes (56). Several preventive interventions for different target groups were compared in this study. In general, the cost-effectiveness of (theoretical) interventions was more favorable in groups with impaired glucose tolerance compared with mixed populations. However, lifestyle interventions appeared to be highly cost-effective in all target groups and were more effective than surgery for the severely obese. Lifestyle interventions have also been shown to be more cost-effective than metformin treatment for the primary prevention of diabetes (57).

With respect to the potential impact of community-based lifestyle programs, a recent study showed that, theoretically, diabetes incidence could fall by 20% if the entire (U.K.) population were able to meet one more of the five predefined “diabetes healthy behavior prevention goals” related to BMI, diet, and physical activity (15). BMI and physical activity had the largest impact on diabetes incidence, and the authors suggested that even small shifts of the entire population toward more healthy behavior (through population-level interventions) would reduce diabetes incidence. Based on more realistic assumptions about potential effects on just BMI and physical inactivity, the community program in our study would prevent between 0.4 and 2.4% of the diabetes incidence in 20 years if the entire Dutch population were to be reached by the intervention. Although the average lifetime health benefits per individual were relatively low (a gain of a few days in good health), health benefits may be substantial for individuals whose risk factor levels are actually changed.

Several comments need to be made with respect to the generalizability of the

results obtained from our study. First, cost-effectiveness of lifestyle interventions differs among countries because of country-specific intervention and health care costs (17). Although the per individual intervention costs of the health care intervention in our study (€700) were much lower than the intervention costs calculated for the U.S. DPP (~€2,000 if screening costs for impaired glucose tolerance are not considered) (54), they compare well to the costs of other lifestyle interventions within health care as reported in a recent review (27). Costs of diabetes care in the Netherlands appear to be relatively low compared with those in other (European) countries (58). Second, the potential impact of large-scale implementation of interventions depends on risk factor distributions. For example, one of four U.S. adults is considered obese, and so there is a large potential target population for health care interventions. Third, the efficiency of lifestyle interventions may also differ due to country-specific risk factor prevalence; a community-based program with the aim of increasing physical activity might be more cost-effective in, for example, the U.S., where the prevalence of physical inactivity is three times as high as in the Netherlands (59).

In summary, both an intensive lifestyle intervention implemented in a health care setting and targeted to individuals at increased risk of developing diabetes and a community-based lifestyle intervention for the general population are effective in reducing diabetes incidence. Although the average lifetime health benefit per individual for the community intervention is relatively low, health gains on a population level may be substantial when the intervention is implemented on a large scale. Both kinds of lifestyle interventions are cost-effective ways to curb the growing burden of diabetes.

Acknowledgments—We thank Pieter van Baal and Talitha Feenstra for the critical reading of our article.

References

1. Field AE, Manson JE, Laird N, Williamson DF, Willett WC, Colditz GA: Weight cycling and the risk of developing type 2 diabetes among adult women in the United States. *Obes Res* 12:267–274, 2004
2. Koh-Banerjee P, Wang Y, Hu FB, Spiegelman D, Willett WC, Rimm EB:

- Changes in body weight and body fat distribution as risk factors for clinical diabetes in US men. *Am J Epidemiol* 159:1150–1159, 2004
3. Weinstein AR, Sesso HD, Lee IM, Cook NR, Manson JE, Buring JE, Gaziano JM: Relationship of physical activity vs body mass index with type 2 diabetes in women. *JAMA* 292:1188–1194, 2004
4. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC: Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 345:790–797, 2001
5. Hu FB, Leitzmann MF, Stampfer MJ, Colditz GA, Willett WC, Rimm EB: Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. *Arch Intern Med* 161:1542–1548, 2001
6. Will JC, Galuska DA, Ford ES, Mokdad A, Calle EE: Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study. *Int J Epidemiol* 30:540–546, 2001
7. Koppes LLJ, Dekker JM, Hendriks HFJ, Bouter LM, Heine RJ: Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies. *Diabetes Care* 28:719–725, 2005
8. Carlsson S, Hammar N, Grill V: Alcohol consumption and type 2 diabetes meta-analysis of epidemiological studies indicates a U-shaped relationship. *Diabetologia* 48:1051–1054, 2005
9. van Dam RM, Hu FB: Coffee consumption and risk of type 2 diabetes: a systematic review. *JAMA* 294:97–104, 2005
10. Hartemink N, Boshuizen HC, Nagelkerke NJ, Jacobs MA, van Houwelingen HC: Combining risk estimates from observational studies with different exposure cut-points: a meta-analysis on body mass index and diabetes type 2. *Am J Epidemiol* 163:1042–1052, 2006
11. Diabetes Prevention Program Research Group, Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403, 2002
12. Lindstrom J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, Uusitupa M, Tuomilehto J, the Finnish Diabetes Prevention Study Group: The Finnish Diabetes Prevention Study (DPS): lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care* 26:3230–3236, 2003
13. Eriksson KF, Lindgärde F: Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. *Diabetologia* 34:891–898, 1991
14. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP,

- Zheng H, Zhang H, Bennett PH, Howard BV: Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care* 20:537–544, 1997
15. Simmons RK, Harding AH, Jakes RW, Welch A, Wareham NJ, Griffin SJ: How much might achievement of diabetes prevention behaviour goals reduce the incidence of diabetes if implemented at the population level? *Diabetologia* 49:905–911, 2006
 16. Herman WH, Hoerger TJ, Brandle M, Hicks K, Sorensen S, Zhang P, Hamman RF, Ackermann RT, Engelgau MM, Ratner RE, 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* 142:323–332, 2005
 17. Palmer AJ, Roze S, Valentine WJ, Spinaz GA, Shaw JE, Zimmet PZ: Intensive lifestyle changes or metformin in patients with impaired glucose tolerance: modeling the long-term health economic implications of the diabetes prevention program in Australia, France, Germany, Switzerland, and the United Kingdom. *Clin Ther* 26:304–321, 2004
 18. Davey Smith G, Bracha Y, Svendsen KH, Neaton JD, Haffner SM, Kuller LH, the Multiple Risk Factor Intervention Trial Research Group: Incidence of type 2 diabetes in the randomized multiple risk factor intervention trial. *Ann Intern Med* 142:313–322, 2005
 19. Zimmet P, Shaw J, Alberti KG: Preventing type 2 diabetes and the dysmetabolic syndrome in the real world: a realistic view. *Diabet Med* 20:693–702, 2003
 20. Vijgen SM, Hoogendoorn M, Baan CA, de Wit GA, Limburg W, Feenstra TL: Cost effectiveness of preventive interventions in type 2 diabetes mellitus: a systematic literature review. *Pharmacoeconomics* 24: 425–441, 2006
 21. Wing RR, Venditti E, Jakicic JM, Polley BA, Lang W: Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes Care* 21:350–359, 1998
 22. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, Smith WC, Jung RT, Campbell MK, Grant AM: Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess* 8:iii–iv, 1–182, 2004
 23. Hoogenveen RT, Feenstra TL, van Baal PHM, Baan CA: *A Conceptual Framework for Budget Allocation in the RIVM Chronic Disease Model—A Case Study of Diabetes Mellitus*. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2005
 24. Kahn EB, Ramsey LT, Brownson RC, Heath GW, Howze EH, Powell KE, Stone EJ, Rajab MW, Corso P: The effectiveness of interventions to increase physical activity: a systematic review. *Am J Prev Med* 22:73–107, 2002
 25. Verheijden MW, Kok FJ: Public health impact of community-based nutrition and lifestyle interventions. *Eur J Clin Nutr* 59 (Suppl. 1):S66–S75; discussion S76, 2005
 26. McTigue KM, Harris R, Hemphill B, Lux L, Sutton S, Bunton AJ, Lohr KN: Screening and interventions for obesity in adults: summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 139:933–949, 2003
 27. Bogers RP, Vijgen SMC, Bemelmans WJE: *Costs of Lifestyle Interventions within Health Care and the Amount of Weight Loss Achieved*. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2006
 28. Taylor CB, Fortmann SP, Flora J, Kayman S, Barrett DC, Jatulis D, Farquhar JW: Effect of long-term community health education on body mass index: the Stanford Five-City Project. *Am J Epidemiol* 134: 235–249, 1991
 29. Brownson RC, Smith CA, Pratt M, Mack NE, Jackson-Thompson J, Dean CG, Dabney S, Wilkerson JC: Preventing cardiovascular disease through community-based risk reduction: the Bootheel Heart Health Project. *Am J Public Health* 86: 206–213, 1996
 30. Goodman RM, Wheeler FC, Lee PR: Evaluation of the Heart To Heart Project: lessons from a community-based chronic disease prevention project. *Am J Health Promot* 9:443–455, 1995
 31. Bemelmans WJE, Wendel-Vos GCW, Bos G, Schuit AJ, Tijhuis MAR: *Interventions to Prevent Overweight in a Community Setting, at School, at Work or in a Health Care Setting: Exploring the Results*. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2004 [in Dutch]
 32. O'Loughlin JL, Paradis G, Gray-Donald K, Renaud L: The impact of a community-based heart disease prevention program in a low-income, inner-city neighborhood. *Am J Public Health* 89:1819–1826, 1999
 33. 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 Syst Rev* CD005270, 2005
 34. Schuit AJ, Wendel-Vos GC, Verschuren WM, Ronckers ET, Ament A, van Assema P, van Ree J, Ruland EC: Effect of 5-year community intervention Hartslag Limburg on cardiovascular risk factors. *Am J Prev Med* 30:237–242, 2006
 35. Ronckers ET, Groot W, Steenbakkers M, Ruland E, Ament A: Costs of the 'Hartslag Limburg' community heart health intervention. *BMC Public Health* 6:51, 2006
 36. Mensink M, Feskens EJM, Saris WHM, de Bruin TWA, Blaak EE: Study on Lifestyle Intervention and Impaired Glucose Tolerance Maastricht (SLIM): preliminary results after one year. *Int J Obes Relat Metab Disord* 27:377–384, 2003
 37. Mensink M, Blaak EE, Corpeleijn E, Saris WH, de Bruin TW, Feskens EJ: Lifestyle intervention according to general recommendations improves glucose tolerance. *Obes Res* 11:1588–1596, 2003
 38. Feenstra TL, Hamberg-van Reenen HH, Hoogenveen RT, Rutten-van Molken MP: Cost-effectiveness of face-to-face smoking cessation interventions: a dynamic modeling study. *Value Health* 8:178–190, 2005
 39. Hoogenveen RT, Feenstra TL, van Baal PHM, Baan CA: *A Conceptual Framework for Budget Allocation in the RIVM Chronic Disease Model: A Case Study of Diabetes Mellitus*. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2005
 40. Feenstra TL, van Genugten ML, Hoogenveen RT, Wouters EF, Rutten-van Molken MP: The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: a model analysis in the Netherlands. *Am J Respir Crit Care Med* 164:590–596, 2001
 41. Hoogendoorn M, Rutten-van Molken MP, Hoogenveen RT, van Genugten ML, Buist AS, Wouters EF, Feenstra TL: A dynamic population model of disease progression in COPD. *Eur Respir J* 26:223–233, 2005
 42. Struijs JN, van Genugten MLL, Evers SMAA, Ament AJHA, Baan CA, van de Bos GAM: Modeling the future burden of stroke in the Netherlands: impact of aging, smoking, and hypertension. *Stroke* 36:1648–1655, 2005
 43. Baan CA, Bos G, Jacobs-van der Bruggen MAM: *Modeling Chronic Disease: The Diabetes Module*. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2005
 44. van Kreijl CF, Knaap AGAC, van Raaij JMA: *Our Food, Our Health. Healthy Diet and Safe Food in the Netherlands*. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2006
 45. Polder JJ, Takken J, Meerding WJ, Kommer GJ, Stokx LJ: *Costs of Illness Study in the Netherlands* [in Dutch]. Bilthoven, Netherlands, National Institute for Public Health and the Environment, 2002
 46. van Baal PHM, Feenstra TL, Hoogenveen RT, de Wit GA: *Cost Effectiveness Analysis with the RIVM Chronic Disease Model*. Bilthoven, Netherlands, Dutch National Institute for Public Health and the Environment, 2005
 47. Melse JM, Essink-Bot ML, Kramers PGN, Hoeymans N, the Dutch Burden of Disease

- Group: A national burden of disease calculation: Dutch disability-adjusted life-years. *Am J Public Health* 90:1241–1247, 2000
48. Stouthard MEA, Essink-Bot M-L, Bonsel GJ, the Dutch Disability Weights Group: Disability weights for diseases—a modified protocol and results for a Western European region. *Eur J Pub Health* 10:24–30, 2000
49. Lopez AD, Murray CC: The global burden of disease, 1990–2020. *Nat Med* 4:1241–1243, 1998
50. van Baal PH, Hoeymans N, Hoogenveen RT, de Wit GA, Westert GP: Disability weights for comorbidity and their influence on health-adjusted life expectancy. *Popul Health Metr* 4:1, 2006
51. College voor zorgverzekeringen: *Guidelines for Farmaco-Economic Evaluations, Actualised Version* [in Dutch]. Diemen, Netherlands, College voor zorgverzekeringen, 2006
52. Casparie AF, van Hout BA, Simoons ML: Guidelines and costs. *Ned Tijdschr Geneesk* 142:2075–2077, 1998 [in Dutch]
53. Simoons ML, Casparie AF: Therapy and prevention of coronary heart diseases through lowering of the serum cholesterol levels; third consensus 'Cholesterol.' Consensus Working Group, CBO. *Ned Tijdschr Geneesk* 142:2096–2101, 1998 [in Dutch]
54. Hernan WH, Brandle M, Zhang P, Williamson DF, Matulik MJ, Ratner RE, Lachin JM, Engelgau MM, the Diabetes Prevention Program Research Group: Costs associated with the primary prevention of type 2 diabetes mellitus in the diabetes prevention program. *Diabetes Care* 26:36–47, 2003
55. Stevens VJ, Obarzanek E, Cook NR, Lee IM, Appel LJ, Smith West D, Milas NC, Mattfeldt-Beman M, Belden L, Bragg C, Millstone M, Raczynski J, Brewer A, Singh B, Cohen J: Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Ann Intern Med* 134:1–11, 2001
56. Segal L, Dalton AC, Richardson J: Cost-effectiveness of the primary prevention of non-insulin dependent diabetes mellitus. *Health Promot Int* 13:197–209, 1998
57. The Diabetes Prevention Program Research Group: Within-trial cost-effectiveness of lifestyle intervention or metformin for the primary prevention of type 2 diabetes. *Diabetes Care* 26:2518–2523, 2003
58. Jönsson B: Revealing the cost of type II diabetes in Europe. *Diabetologia* 45:S5–S12, 2002
59. Centers for Disease Control and Prevention (CDC): Trends in leisure-time physical activity by age, sex and race/ethnicity—United States, 1994–2004. *Morb Mortal Wkly Rep* 54:991–994, 2005