Diet or diet plus physical activity in patients with early type 2 diabetes

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England.” This means good-quality research that is carefully designed and thoughtfully constructed—something we have yet to see in this area.

We declare that we have no conflicts of interest.

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- 1 Bloom N, Cooper Z, Gaynor M, et al. In defence of our research on competition in England's National Health Service. *Lancet* 2011; published online Nov 8. DOI:10.1016/S0140-6736(11)61708-X.
- 2 Propper C, Burgess S, Gossage D. Competition and quality: evidence from the NHS internal market 1991–1996. *Econ J* 2008; **118**: 138–70.
- 3 Pollock A, Macfarlane A, Kirkwood G, et al. No evidence that patient choice in the NHS saves lives. *Lancet* 2011; published online Oct 10. DOI:10.1016/S0140-6736(11)61553-5.
- 4 West RM, Cattle BA, Bouyssie M, et al. Impact of hospital proportion and volume on primary percutaneous coronary intervention performance in England and Wales. *Eur Heart J* 2011; **32**: 706–11.
- 5 Imbens G, Wooldridge J. Recent developments in the econometrics of program evaluation. *J Econ Lit* 2009; **47**: 5–86.
- 6 Angrist JD, Pischke J-S. The credibility revolution in empirical economics: how better research design is taking the con out of econometrics. *J Econ Persp* 2010; **24**: 3–30.
- 7 Bevan G, Skellern M. Does competition between hospitals improve clinical quality? A review of evidence from two eras of competition in the English NHS. *BMJ* 2011; **343**: d6470.

Diet or diet plus physical activity in patients with early type 2 diabetes

R C Andrews and colleagues (July 9, p 129)¹ state as their final interpretation that “The addition of an activity intervention conferred no additional

benefits.” However, this conclusion is misleading, since the achieved increases in physical activity in the diet plus activity group were insufficient to support it.

In fact, although only one group was instructed to do physical activity, no clinically relevant difference was noted in moderate-to-vigorous physical activity versus the “non-sedentary” control and diet intervention groups (31 min vs 26 min and 27 min, respectively, by accelerometry). The within-group increase from baseline in the diet plus physical activity group was also small (from 23 min to 31 min). We question how such a slight difference in physical activity level could have produced significant effects.

Moreover, no difference between groups was found in sedentary time, minimisation of which could be as important as physical activity for improving cardiovascular risk factors.² In our opinion, the lack of additional benefits in the diet and physical activity group is due to the insufficient increase in volume and intensity of physical activity. Previous randomised trials^{3–5} have clearly shown the beneficial effects of physical activity or exercise, independent of disease duration, contrary to Andrews and colleagues’ interpretation in their Research in Context panel.

We declare that we have no conflicts of interest.

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- 1 Andrews RC, Cooper AR, Montgomery AA, et al. Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. *Lancet* 2011; **378**: 129–39.

- 2 Healy GN, Wijndaele K, Dunstan DW, et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Diabetes Care* 2008; **31**: 369–71.
- 3 Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med* 2007; **147**: 357–69.
- 4 Balducci S, Zanuso S, Nicolucci A, et al, for the Italian Diabetes Exercise Study (IDES) Investigators. Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in type 2 diabetic subjects. A randomized controlled trial: the Italian Diabetes and Exercise Study (IDES). *Arch Intern Med* 2010; **170**: 1794–803.
- 5 Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 2010; **304**: 2253–62.

The Early ACTID trial¹ shows that a dietary intervention in patients with early diagnosed type 2 diabetes is as effective in reducing glycated haemoglobin (HbA_{1c}) and blood pressure as is diet plus physical activity. Thus, R C Andrews and colleagues conclude that additional efforts needed to combine dietary advice with advice on physical activity are not justified. Although this conclusion is appropriate in the context of the trial, inclusion of a group doing physical activity only, along with more sophisticated metabolic phenotyping, would have been needed to explore the genuine significance of physical activity treatment for (pre)diabetes.

Muscle insulin resistance is an early detectable hallmark in the pathogenesis of type 2 diabetes that coincides with mitochondrial dysfunction, even in the normoglycaemic prediabetic state.² This finding is partly reflected in reduced metabolic flexibility—the ability to adapt fuel selection to substrate availability (ie, post-prandial vs fasted conditions)—in the insulin-resistant state. In patients with long-standing (>3 years) type 2 diabetes, exercise training without intentional weight loss restored metabolic flexibility.³ Improved metabolic flexibility was only noted when exercise and diet

were combined and not when diet was the sole intervention.⁴

24 h of continuous glucose monitoring revealed that even a single exercise session reduces cumulative episodes of hyperglycaemia by about 50%,⁵ and improved metabolic flexibility through training also favours post-prandial glucose handling.

The setting of the Early ACTID trial complicates testing these favourable adaptations. Thus, generalisation of the trial outcome might have the unwarranted side-effect of under-recognition of the power of physical activity in prevention and treatment of early diagnosed type 2 diabetes. Long-term adherence to dietary and physical activity interventions and their combination requires support by well trained health-care workers anyhow. So, why not teach health-care professionals the convincing beneficial effects of exercise?

We declare that we have no conflicts of interest.

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- 1 Andrews RC, Cooper AR, Montgomery AA, et al. Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. *Lancet* 2011; **378**: 129–39.
- 2 Phielix E, Schrauwen-Hinderling VB, Mensink M, et al. Lower intrinsic ADP-stimulated mitochondrial respiration underlies in vivo mitochondrial dysfunction in muscle of male type 2 diabetic patients. *Diabetes* 2008; **57**: 2943–49.
- 3 Meex RC, Schrauwen-Hinderling VB, Moonen-Kornips E, et al. Restoration of muscle mitochondrial function and metabolic flexibility in type 2 diabetes by exercise training is paralleled by increased myocellular fat storage and improved insulin sensitivity. *Diabetes* 2010; **59**: 572–79.
- 4 Amati F, Dube JJ, Shay C, Goodpaster BH. Separate and combined effects of exercise training and weight loss on exercise efficiency and substrate oxidation. *J Appl Physiol* 2008; **105**: 825–31.
- 5 Manders RJ, Van Dijk JW, van Loon LJ. Low-intensity exercise reduces the prevalence of hyperglycemia in type 2 diabetes. *Med Sci Sports Exerc* 2010; **42**: 219–25.

Authors' reply

Objective measurement of physical activity in ACTID by use of accelerometers showed that we achieved an increase in activity at 6 and 12 months in the diet and activity group compared with the diet only or usual care groups (see original table 3). This increase in activity was similar to that seen in both the Finnish and American diabetes prevention studies and many other beneficial non-supervised exercise studies in patients with diabetes.^{1–3} This increase equated to 9 min per day or more than 1 h per week of additional exercise—an increase of 30% in the diet and activity group.

Compliance with exercise, as measured by pedometer, was also very good, with an increase of 20% seen in overall daily steps between baseline and 6 months (6399 [SD 3056] to 7680 [2818]), which was maintained to 12 months and consistent with the 29.9% increase seen in a meta-analysis of pedometer intervention studies.⁴ Hence lack of performance of the exercise or lack of difference in increased physical activity between the intervention groups is unlikely to explain our findings. The remaining possible interpretations of our results therefore include that participants in the diet and activity group made fewer changes to their diet than did those focusing on diet alone, or that the form of exercise used (similar to that in other unsupervised intervention trials) was not ideal.

Populations involved in supervised exercise programmes, in whom the benefits have most consistently been shown, tend to be more select, younger, have worse diabetes control, have had diabetes for longer, and have substantially more contact time than the population in the ACTID Study. These studies were also not designed to answer the specific question that ACTID set out to answer, namely if you give advice on diet and exercise together, in a real-world, community-based cohort in the first year after diagnosis, is this more effective than giving advice on diet alone? We specifically chose an

unsupervised intervention, since with the large numbers of affected patients, resources are unlikely to be available to provide supervised interventions to all patients. Even in an intense supervised exercise programme, aerobic training alone, the form of exercise used in ACTID, does not improve glucose control,⁵ and the most recent review of physical activity in patients with diabetes found that non-supervised exercise is only beneficial if given with dietary advice.⁵

A physical activity alone group, along with more sophisticated metabolic phenotyping, would have enabled us to explore in more detail the effects of this treatment in patients with newly diagnosed diabetes. This was not the aim of ACTID. We aimed to determine whether, in current health-care systems, where greater investments are being made into education programmes to improve patients' diets, there is additional benefit of giving exercise advice over and above comprehensive dietary advice.

Our conclusions were not intended to erode health-care workers' views on physical activity—we too are enthusiasts for increases in physical activity. Rather, they were intended as a “call to arms” for us to invest further in dietary interventions and rigorous pragmatic trials in this area, recognising that what is effective in routine health care is often different from what is effective in more highly controlled mechanistic studies.

RCA has received honoraria from GlaxoSmithKline, Novo Nordisk, Sanofi-Aventis, and Lilly, and travel expenses from Sanofi-Aventis. CMD has received consultancy fees from GlaxoSmithKline and Medtronic Advisory, speaker's fees from Novo Nordisk and Bristol-Myers Squibb, travel expenses from Medtronic, and is named on a patent held by Novartis. The other authors declare that they have no conflicts of interest.

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