



Lifestyle interventions in preventing new type 2 diabetes in Asian populations

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Abstract The aim of this study was to review current evidence on interventional studies aimed at the prevention of type 2 diabetes in Asian population with lifestyle interventions. Prevalence of type 2 diabetes sharply increased in most Asian countries during the last decades. This issue has now also relevant implication for Europe where different surveys are also consistently revealing an higher prevalence of type 2 diabetes and other and major CVD risk factors among subjects originating from Asian Countries than in the native population. Nutrition and lifestyle transition seem to play a role in disclosing the predisposition for the development of type 2 diabetes and great interest is now shown toward the possibility to intervene with lifestyle intervention on at risk populations. A meta-analysis of Randomized Controlled Trials showed that lifestyle interventions are highly effective also in the Asian population. All studies were, however, conducted with an individual approach based on the identification of high-risk individuals. When ethnic minority groups have to be addressed, an approach directed to the community rather than to the individual might, however, be

more effective. This review reinforces the importance for policy-makers to consider the involvement of the whole community of minority immigrant groups with lifestyle intervention programs.

Keywords Type 2 diabetes prevention · Ethnicity · Ethnic minority groups · IDF geographical regions · Meta-analysis

Diabetes in Asia; which implications for Europe?

Asia is the epicentre of the global epidemic of type 2 diabetes mellitus (T2DM) [1]. Over 138 million people with diabetes live in the Western Pacific area (98.4 million in China) and 72 million in the South-East Asia area (65.1 million in India). Most Asian countries experienced a relevant nutrition and lifestyle transition in the past few decades that played a role in disclosing the predisposition of Asian populations to the development of T2DM. China presented an innovative approach showing the importance of lifestyle intervention in the prevention of T2DM [2]. Other studies in the USA, Finland, Japan and India reached similar rates of success [3–6]. In the same line, the importance of physical exercise is now recognized in prevention, and the discipline of sports medicine has begun to widen its interests from athletes to cardiovascular and metabolic diseases in populations [7–9]. The current T2DM epidemic might thus be limited, and sustainable programs have been launched at national levels [10–16].

Changes occurring in Asian countries have now implications also for Europe where a high prevalence of T2DM is observed among Asian migrants originating from India, Pakistan, Bangladesh, Sri Lanka, Nepal, Bhutan and the Maldives [17–20]. For the majority of European countries,

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where immigration is a recent phenomenon, a common assumption is that health promotion interventions effective in the general population are also effective in ethnic minorities. Therefore, only a few countries specifically consider minority groups in their national health plans for metabolic and cardiovascular prevention. Cultural factors may, however, limit the ability of interventions addressed at the native population to reach minority groups [21]. The current relevant wave of immigration requires implementation of prevention strategies specifically addressed to minority ethnic groups [22].

Ethnic origin and the risk of type 2 diabetes

Overweight and obesity are the main risk factors for the development of new T2DM, and the importance of body weight control is well recognized in prevention [21, 23]. Modest weight loss (5–10 % of body weight) and modest physical activity (30 min daily) indeed offer a variety of benefits in addition to the possibility of preventing or delaying T2DM [21]. Rendering targeted advice to at-risk individuals is thus especially imperative for physicians. The main question is: Who is to be considered at high risk? Subjects originating from South Asia, China, and Africa develop T2DM at a higher rate, at an earlier age, and at lower ranges of BMI than their European counterparts [24]. A clustering of different genetic defects or polymorphisms, the “thrifty gene” hypothesis, a genetic susceptibility to insulin resistance and higher central adiposity at similar BMI levels, or epigenetic changes occurring during gestation, might play a role in influencing metabolic phenotypes of Asian populations [25–27]. For these reasons, the WHO consultation group recommends a lower cutoff of BMI for Asians with respect to native European populations [28]. The identified diagnostic cutoff for being overweight is 23 kg/m² in India, and 24 kg/m² in China [29, 30]. Proper consideration of this issue by European physicians when facing these new patients in their offices might increase opportunities for education, intervention, and behaviour and lifestyle changes [31]. However, the main scientific societies in Europe still give little attention to the different cutoffs for overweight of ethnic minorities [21].

Furthermore, although ethnic origin has a value “per se” in the estimation of the risk for T2DM, doctors often base their prediction on blood glucose measured at opportunistic screening [32–36]. The risk of developing T2DM is over 5 times higher in subjects with impaired glucose tolerance (IGT) being 12 times higher in those with both IGT and impaired fasting glucose (IFG) compared to normoglycemic individuals [37]. However, blood glucose has limitations because (1) it is an invasive, costly, and time

consuming procedure; (2) it has a large random variation; (3) when taken in the aggregate, age, family history of T2DM, ethnicity, waist-to-hip ratio, BMI, blood pressure, and lipid levels, combined with plasma glucose levels are more predictive of future T2DM than glucose levels by themselves; (4) most importantly, the opportunities for an immigrant to have a blood test may be low, because of cultural barriers (varying rates of literacy, limited motivation linked to the lack of education on healthy lifestyle) and socioeconomic status [38–40]. Finally, primary prevention should be addressed at high-risk subjects when they are still in a normoglycemic state, and interventions should prevent their transition from normoglycemia to IFG and IGT. For these reasons, inexpensive, easily administered, cost-effective, and validated non-invasive risk scores (based on non-laboratory clinical variables) have been made available [41, 42]. These non-invasive scores identify a high risk of T2DM (*C* statistics ≥ 0.8) with acceptable to good discriminatory power across diverse settings in Europe [42–47]. Five non-invasive scores, the ARIC 2005, ARIC 2009, AUSDRISK, DPoRT, and QD Score, include the ethnic origin in the model [48–52]. To screen subjects at risk for T2DM, the American Diabetes Association (ADA) currently recommends a non-invasive tool that includes ethnicity (available at the URL: <http://www.ndep.nih.gov/am-i-at-risk/diabetes-risk-test.aspx>). A study performed in the USA compared three risk scores in a multi-ethnic population living in the same country [53]. In Europe, non-invasive tools were validated in different settings, although none of the diverse setting included ethnic minority groups [42].

The possibility of preventing T2DM was demonstrated in different studies, all including subjects on the basis of blood glucose values [54]. Some randomized controlled clinical trials were specifically conducted in Asian populations.

Lifestyle interventions and prevention of type 2 diabetes in Asian populations

PUBMED and EMBASE were systematically searched for randomized controlled clinical trials investigating the effect of lifestyle interventions in preventing new T2DM in Asian populations. Eligible studies were controlled randomized clinical trials performed in Asian populations, reporting incidence of new cases of T2DM, whatever the duration of the study, published between 1994 and December 2014. Randomized clinical trials including patients with diabetes and duplicate publications or sub-studies of included trials were excluded. Two investigators independently abstracted the data from the eligible studies. Disagreements were resolved via consensus. Search was

conducted using terms, including type 2 diabetes mellitus, non-insulin-dependent diabetes, prevention, pre-diabetes, impaired fasting glucose (IFG), IGT, obesity, and lifestyle modification, limiting search to randomized controlled clinical trials and human studies. A manual search was also performed on reference lists from articles, reviews, and editorials. The measure of the effect of treatment was the difference in the incidence of new cases of T2DM in the intervention group and in the control group. For each study included in the meta-analysis, the incidences of T2DM in the control group and intervention group were used to process the forest plot. Intervention effect (new cases of T2DM) was expressed as odds ratio (OR), with 95 % confidence intervals (CIs); meta-analysis was performed by a random-effects model. Heterogeneity was examined with the I^2 , where I^2 values of 75 % or more indicated a high level of heterogeneity. The meta-analysis followed the PRISMA Checklist (Supplemental information) and was conducted using Rev Man 5.0 software (Fig. 1).

Eight randomized controlled clinical trials studies evaluated diet and physical activity interventions in Asian adults [2, 5, 6, 55–59]. The main characteristics of the included studies are reported in Table 1. The eight prospective randomized clinical studies include a total population of 2721 subjects at high risk for T2DM. All T2DM prevention trials performed in Asian populations have been based on a high-risk status defined by blood tests. In all studies, the inclusion criteria indeed required

IGT, assessed with oral glucose tolerance test (OGTT), or IFG [2, 5, 6, 55–59]. All eight RCTs were suitable for inclusion in the meta-analysis showing a 45 % reduction in the incidence of new T2DM in Asian subjects assigned to the intervention arm (OR 0.55; 95 % CI 0.44–0.70) (Fig. 2). Most importantly, a low level of heterogeneity was found among studies performed in different settings (I^2 8 %).

The earliest Chinese study, published in 1997, started activities in 1986 when the prevalence of T2DM in China was still low (1–2 %) [2, 60, 61]. Pan et al. screened 577 men and women with IGT from a sample of 110,660 subjects. Subjects were then randomized to a programme of diet, exercise, or both [2]. Dietary intervention was focused on increased amounts of vegetables and reduced consumption of alcohol and simple sugars; overweight individuals (those with a BMI >25 kg/m²) were encouraged to lose weight. The exercise group was instructed to increase their daily activity by an equivalent of 20 min of moderate activity (brisk walking), and the diet-plus-exercise group was asked to do both exercise and dietary modification. After 6 years of follow-up, all three interventions were similarly effective, with risk reductions of 31–46 % compared to the control group. A recent long-term follow-up shows that the reduction in the 20-year cumulative incidence in the intervention groups (80 vs 93 % in the control group) [62] is paralleled by a reduction in the long-term cumulative incidence of CVD mortality (11.9 % in the intervention group vs 19.6 % in the control group, HR 0.59; 95 % CI 0.36–0.96; $p = 0.033$) and all-cause mortality (28.1 vs 38.4, HR 0.71; 95 % CI 0.51–0.99; $p = 0.049$) [62]. These data are the first available showing the impact on mortality of lifestyle intervention and are of great value in a country where 40 % of subjects aged 19–29 years were recently found to have a blood glucose level in the range of pre-diabetes [63].

In the study by Kosaka et al., 458 Japanese men with IFG and IGT were assigned to lifestyle ($n = 102$) or standard intervention ($n = 356$) [5]. OGTT was repeated every 6 months, and at the 4-year follow-up the cumulative incidence of T2DM was 9.3 and 3.0 % in the control and in the intervention groups, respectively. The reduction in the risk of T2DM is associated with larger body weight reduction (0.39 and 2.18 kg, respectively).

In the Indian Diabetes Prevention Programme (IDPP-1), 10,839 native Asian Indians underwent the screening and IGT was detected in 1027 subjects [6]. 1025 responded when called for a confirmatory OGTT, and a total of 531 subjects diagnosed with IGT on both tests (persistent IGT) were randomized into four groups (standard advice; lifestyle intervention; metformin; lifestyle plus metformin). Lifestyle intervention proved to be effective in this population with a very high 3-year cumulative incidence of

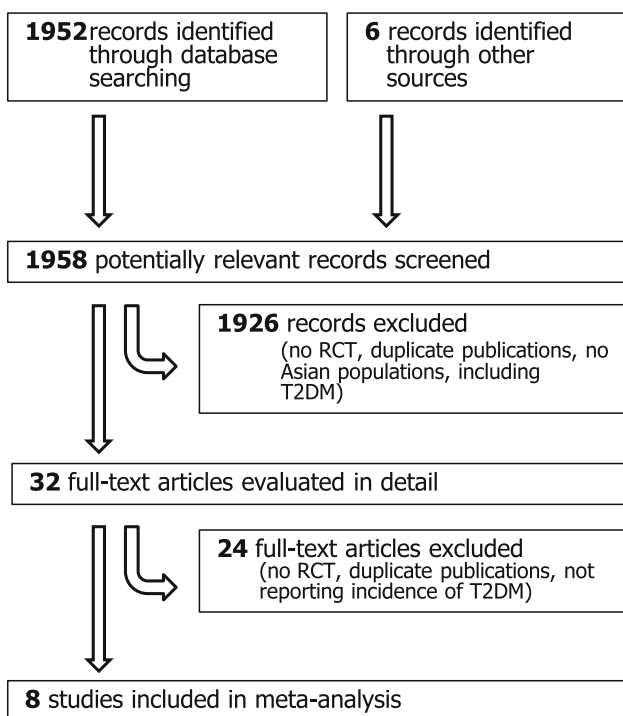


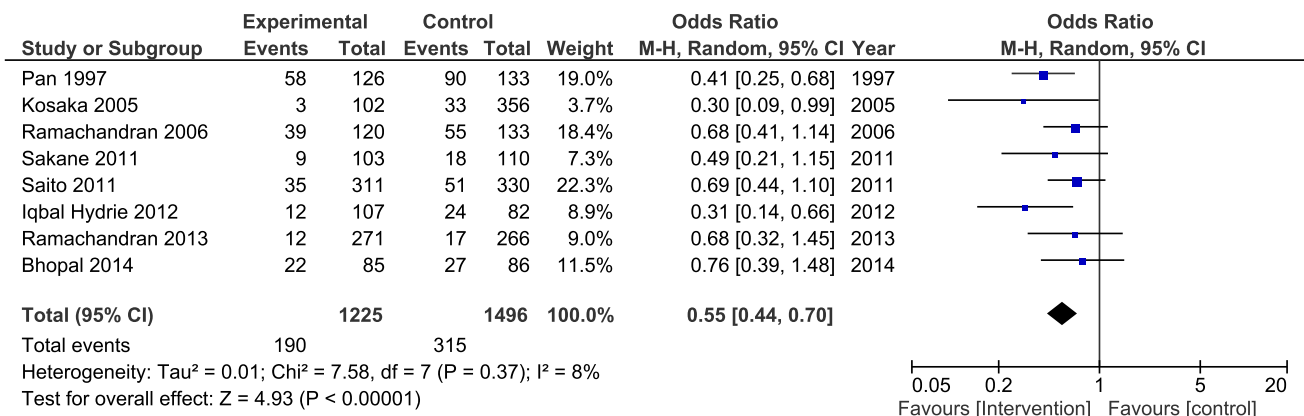
Fig. 1 Selection of studies for the meta-analysis

Table 1 Randomized controlled clinical trials (RCT) performed in Asian populations

Author	Year	Inclusion criteria	Ethnicity (Country)	Duration (months)	Arms	Outcome
Pan et al. [2]	1997	IGT	Chinese (China)	72	Control: general written instructions on diet and physical activity Intervention: personalized instruction and counselling for diet and physical exercise	New type 2 diabetes
Kosaka et al. [5]	2005	Men; IFG and IGT	Japanese (Japan)	48	Control: for BMI 24 kg/m ² , take 5–10 % smaller meals than they had been taking and increase physical activity (lose weight); for BMI <24 kg/m ² avoid gaining weight by diet and exercise Intervention: for BMI ≥22 kg/m ² subjects were informed of their desirable body weight individually (suggestion to reduce weight at a rate of 0.5–1.0 kg/month); for BMI <22 kg/m ² maintain weight and not gain weight	New type 2 diabetes
Ramachandran et al. [6]	2006	IGT on two occasions (persistent IGT)	Indians (India)	30	Control: subjects involved in physical labour, who had to walk or cycle for >30 min/day, or performing exercises regularly, were asked to continue their routine activities. Sedentary subjects were advised and regularly motivated to walk briskly for at least 30 min each day Intervention: subjects received advice on both healthy diet and regular physical activity. Scores were given based on the subjects' adherence. Diet modification including reduction in total calories, refined carbohydrates and fats, avoidance of sugar, and inclusion of fibre-rich foods	New type 2 diabetes
Sakane et al. [56]	2011	IFG and IGT	Japanese (Japan)	36	Control: one group session on a healthy lifestyle and prevention of diabetes. No individual guidance was given during the study period Intervention: specific advice on both healthy diet and regular physical activity. Goals of intervention: reduce body weight by 5 % in overweight and obese subjects, and to increase energy expenditure due to leisure time physical activity by 700 kcal per week. Advise: take the proper amount of calories; decrease the mean percent of energy derived from dietary fat (<25 %); restrict daily alcohol consumption (<160 kcal); eat three meals a day and avoid eating late at night; achieve the exercise goal, aerobic exercise such as walking is recommended	New type 2 diabetes
Saito et al. [55]	2011	Overweight with IFG and IGT	Japanese (Japan)	36	Control: reduce total energy intake and increase physical activity (5 % reduction in body weight), through the help of nurses, dieticians, physical therapists, and physicians. Instructions: four times at 12-month intervals Intervention: reduce total energy intake and increase physical activity (5 % reduction in body weight), through the help of nurses, dieticians, physical therapists, and physicians. Individual instructions and follow-up support from the medical staff at least nine times. Follow-up visits and use of self-monitoring sheets for recording body weight, pedometer counts, and how close they came to attaining their goals. Dietary intervention: reduce total energy intake mainly by restricting excess intake of fat or carbohydrates (fat intake at 20–25 % of total energy intake; carbohydrate intake at 55–60 % of total energy intake)	New type 2 diabetes

Table 1 continued

Author	Year	Inclusion criteria	Ethnicity (Country)	Duration (months)	Arms	Outcome
Iqbal Hydrie et al. [57]	2012	Age >30 years; IGT	Pakistani (Pakistan)	18	Control: subjects received general diet and exercise information at baseline and at subsequent visits; no intensive individual specific counselling was given Intervention: training sessions and counselling were given to subjects in the intervention group about intervention goals (body weight loss $\geq 5\%$ via diet control and physical exercise, total fat intake <30% of energy consumed, fibre intake of 15 g/1000 kcal, and moderate exercise >30 min/day). Sessions with dietitians and physical trainers at each visit and individual counselling to increase physical activity (endurance exercises such as walking, jogging, and cycling)	New type 2 diabetes
Ramachandran et al. [58]	2013	Men; owning a mobile phone; familial history of type 2 diabetes; BMI >23 kg/m ² ; IGT	Indians (India)	20	Control: personalized education and motivation about health lifestyle principles, and written information about diet and physical activity Intervention: in addition, a manager website delivered cyclically phone message reminders (2–4 message per week, not the same message in a 6-month period)	New type 2 diabetes
Bhopal et al. [59]	2014	IFG; IGT; waist: >90 cm M or >80 cm in W	South Asians (UK)	36	Control: standardized written and verbal advice Intervention: consultation with a dietitian (both participants and family volunteers were part of this intervention) with 15 visits over 3 years (baseline, monthly for the first 3 months, then every 3 months) on achieving weight loss through a calorie-deficit diet and physical activity (>30 min daily brisk walking), using culturally adapted and translated resources (information on shopping and cooking; 3-day food diaries; dietary patterns questionnaire). Annual group sessions, including a food shopping tour and brisk walking. Pedometers were given to provide step counts for motivation through self-monitoring and for the dietitians to assess progress. Bodyweight and waist circumference data were used as motivational devices by dietitians	Weight change at 3 years

**Fig. 2** Odds ratio for the reduction of type 2 diabetes in randomized clinical trials which evaluated the effects of non-pharmacologic lifestyle interventions (physical exercise and diet) in Asian adults

T2DM (55, 39, 40 and 39 % in groups 1–4, respectively) [6].

Sakane et al. performed a lifestyle intervention program in a primary health-care setting on 304 middle-aged Japanese subjects with IGT [56]. The 3-year cumulative incidence tended to be lower in the intervention group (14.8 vs 8.2 %).

The incidence of T2DM was high in the 641 Japanese overweight subjects (aged 30–60 years) with IFG and IGT enrolled by Saito et al. [55]. At 36 months follow-up, the estimated cumulative incidences of T2DM were 12.2 % in the frequent intervention group ($n = 311$) and 16.6 % in the control group ($n = 330$).

In the study performed in Pakistan by Iqbal Hydrie et al., 5000 people attended screening camps where 2300 persons filled the questionnaire and 1825 subjects were identified to be at high risk [57]. Of the 1739 subjects who took the oral glucose tolerance test, 317 were identified as IGT and randomized into three groups (control; intense lifestyle modification advice; intense lifestyle modification advice and metformin 500 mg twice daily). The overall incidence was 4 cases per 1000 person-months, with an incidence of 8.6 cases in the control group, 2.5 cases in the lifestyle modification advice group, and 2.3 cases in the lifestyle modification advice + drug group. The overall compliance rate was 86 %.

An innovative technological approach based on mobile phone messaging in the prevention of T2DM was explored by Ramachandran et al. who screened male Indian subjects with positive familial history of T2DM or BMI >23 kg/m² before performing the IGT test [45, 58]. In this Indian study, the 537 working Indian men with IGT were randomly allocated to receive mobile phone messages ($n = 271$) or standard care ($n = 266$). All participants received diet and exercise advice at baseline. The cumulative incidence of T2DM was significantly reduced in the intervention group compared with the standard-care group [50 (18 %) of 271 participants vs 73 (27 %) of 266; hazard ratio 0.64, 95 % CI 0.45–0.92; $p = 0.015$]. The trial is the first to report a reduction in the onset of T2DM with a mobile messaging intervention. The investigators recorded a high response rate of 96 % ($n = 517$) with a duration of follow-up of 2 years. The nature of the intervention prevented masking of the participants and field staff; however, the laboratory staff and the principal and co-investigators were masked [58]. If the results of this trial are replicated in other settings, mobile phone messaging might be a practical and affordable way to deliver lifestyle advice to delay or prevent the onset of T2DM.

The first study investigating the effects of lifestyle modifications on progression to T2DM in South Asians (Indian or Pakistani) living in the UK was recently performed by Bhopal et al. [59]. Subjects aged 35 years or

older, with waist circumference 90 cm or greater in men or 80 cm or greater in women ($n = 1319$), were screened by oral glucose tolerance test; 196 (15 %) had IGT or IFG and 171 entered the trial and were randomized to intervention (78 families with 85 participants) or control (78 families with 86 participants). Interestingly, the protocol considered the supporting role of the family as important, because participants in the same family were not randomized separately. At 3 years, progression to T2DM (either doctor diagnosed or by oral glucose tolerance test at 3 years) was observed less frequently in the intervention group (15 %) than the control group (21 %), although the difference was not statistically significant (95 % CI 0.27–1.67; $p = 0.3705$).

This meta-analysis is associated with several important limitations. First, this review is limited to published randomized controlled trials, while observational studies and additional unpublished literature are excluded. Although randomized controlled trials generally provide maximum validity and causal inference, non-randomized studies performed at the community level may have been lost. Second, only one study included in the meta-analysis enrolled Asian subjects living in Europe. Further research is therefore needed to better identify effective interventions for the prevention of T2DM in Asian minority groups living in Europe, an issue now crucial for Europe [64]. Third, we did not include subjects from America or Africa, which may limit the generalizability of our results to African or other populations.

Notwithstanding these limitations, current randomized clinical trials seem to indicate that T2DM can be prevented in Asian individuals who are at high risk. However, when the intervention is targeted at Asian communities living in Europe, some aspects have to be considered.

A new perspective for lifestyle interventions in minority groups: from individual to collectivist goals

The main limitations in the high-risk approach to minority groups are represented by costs of the screening procedure, low compliance at follow-up, and the problematic contact with undocumented migrants.

A comparison of potential screening strategies and subsequent interventions for the prevention and treatment of T2DM was performed by Gillies et al., who considered a hypothetical population of the UK, aged 45 years, at the time of screening [65]. In their estimation, lifestyle intervention strategy shows a small clinical potential benefit in terms of average years spent without T2DM and cases of T2DM prevented, because discounted QALYs gained compared with no screening were 0.09 (0.03–0.17) for

screening and lifestyle interventions. The hypothetical population had 17 % of either IGT or undiagnosed T2DM at the time of screening. However, as noted by Gillies et al., when an increased prevalence of IGT and T2DM are considered, the QALYs decrease, and most importantly the total costs of the screening strategy increase [65]. When the model was run for a South Asian cohort, with high prevalence of T2DM, the results for QALYs were reduced and costs of screening increased. Notwithstanding these limitations, Gillies et al. consider lifestyle interventions to be cost-effective compared with no screening in an “at-risk” population [65].

A recent trial performed in the Netherlands studied the effectiveness of an intensive, culturally targeted lifestyle intervention in general practice for weight status and metabolic profile of South Asians at risk of T2DM [66]. Although T2DM incidence is not included among outcomes, the trial is of great interest because limitations connected with the high-risk approach in minority groups are clearly shown. Low initial response rate and laborious recruitment, high dropout rate, and the lack of effect of the lifestyle intervention on weight change and other metabolic parameters indeed led the authors to raise the question whether the high-risk strategy is the optimal approach to prevent T2DM in minority groups [66]. Admiraal et al. conclude that health gain might be better achieved by focusing on prevention strategies that tackle the high risk of T2DM among South Asians at an earlier stage [67].

The large number of subjects not included in population statistics (hidden population of undocumented migrants) is also often not considered in trials and cost-effectiveness analysis. Approximately, 1.7 million Chinese people are now estimated to live in Europe, mostly in the UK, France, Italy, Germany, and Spain, and migration from China to Europe has now been mainly concentrated in countries of Southern Europe, e.g. Italy and Spain [68]. In China, a prevalence of T2DM of 11.6 %, with over 40 % of young adults (aged 18-to-29 years) at risk was found in 2010 [63, 69]. Should the prevalence of prediabetes and T2DM in the Chinese living in Europe be as high as in China, the prevention of T2DM could be a need for our health system [63, 70]. Many minority patients have difficulty communicating with their health-care providers and other cultural barriers may exist [71]. A qualitative study performed in the UK identifies a main barrier for the Bangladeshi community in the complex value hierarchy of what is accepted to be healthy (small portion size, limited rich and fatty food, regular activity) and what is important for the social norms of hospitality, the religious requirement for modesty, and the cultural rejection of a “sporting” identity or dress (especially for women, older people, and senior members of the society) [72]. Contemporary health

promotion, usually based on assumptions of a self-investment, should thus leave the approach to individuals when the aim is to involve societies with a collectivist history [73]. This paradigm change is now required by an ever-changing society.

On this basis, a new strategic plan aimed at the prevention of new T2DM in the Chinese community settled in Prato has been approved recently in Italy by the Regione Toscana. The project aim is to encourage weight control and physical activity with interventions on the Chinese community. The local Chinese school will be the setting to contact families. The project will include: distribution of the population of Chinese training materials on T2DM and the correct rules on nutrition and lifestyles; training courses on the importance of nutrition in the prevention of T2DM directed at teachers of the Chinese School and to canteen managers of Chinese factories; promotion of physical activity through the creation of sports groups aggregation of Chinese entities for the realization of projects of sport activity (formation of teams with structured training courses, realization of tournaments and amateur competitions). Objectives for action include the reduction of 5 % loss of body weight through the control diet (total intake of fat less than 30 % of energy consumed, fibre intake per day of 15 g/1000 kcal) and the promotion of moderate exercise (30 min/day with resistance exercises such as walking, jogging, and cycling).

Conclusion

The review identifies three issues to be considered in primary care: (1) ethnic origin is an important element for risk assessment of future T2DM, and specific diagnostic cutoffs for overweight have to be considered in general practice; (2) lifestyle interventions are particularly important to reduce the future incidence of T2DM in the Asian population living in Europe; (3) the approach to individual high-risk subjects followed in randomized controlled trials is effective, although limitations exist when pursued in minority groups and a new perspective for an approach specifically involving the whole communities is now needed for Europe.

It is now important to launch public health promotion programs of primary prevention, specifically addressed to minority groups, and the cooperation of ethnic communities is essential. Educational prevention programs are important to limit the development of new T2DM in Europe.

Compliance with ethical standards

Conflict of interest None.

Statement of human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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