

Treatment of type 2 diabetes in youth: An argument for randomized controlled studies

Heather Dean MD FRCPC, *Department of Pediatrics, University of Manitoba, Winnipeg, Manitoba*

H Dean. Treatment of type 2 diabetes in youth: An argument for randomized controlled studies. Paediatr Child Health 1999;10(4):265-270.

In North America, type 2 diabetes occurs in youth (children and adolescents) of specific ethnic backgrounds, including youth of Aboriginal, Hispanic, Asian, Pacific Islander, Japanese and African-American descent. The treatment of youth with type 2 diabetes represents a unique challenge for paediatricians because of physicians' long experience with this disease in adults but its short history in youth. The education and management of type 2 diabetes in youth must recognize the unique developmental, emotional and social issues associated with this age group, as well as the cultural, linguistic, geographic and socioeconomic issues associated with these populations. With the exception of insulin, the drugs used for adults with type 2 diabetes have not been studied in youth. There is an urgent need for long term, multicentre randomized controlled studies of oral drugs for type 2 diabetes in youth.

Key Words: *Oral antihyperglycemic drugs; Type 2 diabetes*

The demographics of type 2 diabetes, previously known as adult-onset diabetes or noninsulin-dependent diabetes mellitus, have changed to include children and adolescents aged six to 18 years (1). In adolescents in North America, type 2 diabetes occurs most often in youth of specific ethnic backgrounds, including youth of Aboriginal, Hispanic, Asian, Pacific Islander, Japanese and African-American descent. In Canada, it has been diagnosed most often in Aboriginal youth in the Canadian provinces of Ontario (northern areas), Manitoba and Saskatchewan (2,3). In large urban centres in Canada, it is likely that type 2 diabetes will also be diagnosed with increasing frequency in children from the above mentioned ethnic groups because of the increase in the incidence of type 2 diabetes in youth from these ethnic groups, as well as the changing demographics of our ur-

Le traitement du diabète de type 2 chez les jeunes : Un argument en faveur d'études aléatoires et contrôlées

RÉSUMÉ : En Amérique du Nord, le diabète de type 2 se manifeste chez les jeunes (enfants et adolescents) d'origines ethniques précises, y compris les jeunes d'ascendance autochtone, hispanique, asiatique, japonaise, afroaméricaine et des îles du Pacifique. Le traitement des jeunes atteints de diabète de type 2 représente un défi particulier pour les pédiatres en raison de la longue expérience des médecins face à cette maladie chez les adultes, mais de son bref historique chez les jeunes. L'éducation et la prise en charge du diabète de type 2 chez les jeunes doit tenir compte des questions relatives au développement, à l'affectivité et à la socialisation reliées à ce groupe d'âge, de même que des questions culturelles, linguistiques, géographiques et socioéconomiques propres à ces populations. À l'exception de l'insuline, les médicaments utilisés chez les adultes pour traiter le diabète de type 2 n'ont pas encore été étudiés chez les jeunes. Des études aléatoires et contrôlées multicentriques à long terme sur les médicaments pris par voie orale dans le traitement du diabète de type 2 chez les jeunes s'imposent.

ban populations. The unique cultural, geographic and linguistic characteristics of affected youth create new challenges and barriers to the management of this disease; consideration of them is vital to achieve successful outcomes.

The history of this new paediatric disease is too short for long term outcome data to be available. The Pima Indians of the Gila Indian Reserve in southern Arizona have been screened for type 2 diabetes every two years from five years of age since the 1960s. Type 2 diabetes was first recognized in children of this population in the 1970s (4), but there was no organized treatment program established until the early 1980s. Long term follow-up of Pima Indians (5) and anecdotal case reports in Canada indicate that microvascular disease is aggressive in type 2 diabetes with onset in youth.

Paediatric endocrinologists assume that type 2 diabetes in children is the same as in adults, and, thus, treatment strategies have been adapted from experience with adults (1,3,6). Lifestyle modification regarding diet and physical activity is the cornerstone of treatment. The challenges to successful lifestyle modification that face adults with type 2 diabetes add to the unique challenges of adolescence. Although there is extensive literature on the use of oral drugs in adults with type 2 diabetes, there are no data on the dosing, efficacy or safety of these drugs in children. Insulin is the only drug licensed for use in children with diabetes in the United States and Canada, but experience with its use in type 2 diabetes in children is limited and poorly documented. There is an urgent need to develop effective treatment strategies to reduce the burden of complications in young adult life. Furthermore, with the increased risk of type 2 diabetes developing in the offspring of mothers with type 2 diabetes during pregnancy, there is an urgent need to break this vicious cycle through primary prevention programs that target adolescent females.

This paper reviews what is known about the potential treatment strategies for type 2 diabetes in youth and discusses the ethical dilemmas of off-label drug use for children. Most of the anecdotal experience with the treatment of type 2 diabetes in Canada relates to Aboriginal youth.

GOALS OF THERAPY

The goals of therapy for youth with type 2 diabetes are adapted from the adult literature. They include achieving and maintaining hemoglobin A1C at less than 7%, achieving and maintaining a healthy weight, and eliminating the symptoms of hyperglycemia. A decrease in hemoglobin A1C of even 1% is associated with an improved outcome. Intensive follow-up is useful in motivating each person with type 2 diabetes to improve fasting blood glucose levels and weight; intensive follow-up also minimizes the cardiovascular risk factors of hypertension and dyslipidemia.

COMMUNITY INVOLVEMENT

No one disputes the importance of having a specialized diabetes education team to support each child with type 1 diabetes and his or her family in order to achieve a sophisticated level of self-care. The community has an important role to play in supporting the emotional well-being of the child with type 1 diabetes, but the community does not play a critical role in the daily maintenance of blood glucose control. However, in the management of children with type 2 diabetes, the extended family and the community have a more direct role to play in helping the adolescent to maintain blood glucose control because they must create a supportive environment that promotes healthy eating habits and physical activity. They are more effective at changing the community environment than health professionals who are not familiar with the community's culture. In a group of Pima

Indian adults, unstructured community activities focusing on Pima history and culture were more effective in promoting adherence to lifestyle modification and glycaemic control than conventional structured diabetes education (7).

INITIAL THERAPY

Most youth with type 2 diabetes are asymptomatic and identified by screening (2). These youth must receive basic education and counselling about diabetes, monitoring blood glucose levels and nonpharmacological treatment with lifestyle modification. The author and staff at the diabetes clinic at Winnipeg Children's Hospital, Winnipeg, Manitoba, recommend that blood glucose levels be tested at least once daily, and results be recorded in a log book so that the teenager may watch the trend in blood glucose levels over time. The fasting blood glucose level is helpful in assessing short term treatment goals; a recommended goal for fasting blood glucose levels is less than 7 mmol/L.

Some youth with type 2 diabetes present with diabetic ketoacidosis (2,8). This may be associated with an intercurrent infection. The initial intravenous and subcutaneous insulin requirements may be very high (greater than 1.5 unit/kg/day), and the resolution of diabetic ketoacidosis may be prolonged. Many youth can be treated with two to six weeks of subcutaneous insulin therapy, followed by an abrupt discontinuation of insulin and the maintenance of acceptable glycaemic control.

A few youths present with classical symptoms of hyperglycemia, including polyuria, nocturia and weight loss with fasting blood glucose levels greater than 15 mmol/L. They may also benefit from a short course of subcutaneous insulin.

NONPHARMACOLOGICAL TREATMENT

Lifestyle modification and counselling

The conventional first-line of therapy, and the cornerstone of *all* therapy of type 2 diabetes, is to change eating habits and increase physical activity. This therapy can be very effective in adolescents in the summer camp environment (9). Fasting blood glucose levels in the 18 to 20 mmol/L range reach the normal range in a few days with vigorous physical activity and supervised healthy meals.

Nonpharmacological treatment requires comprehensive education and behavioural strategies with skills training for children and their parents to change habits. These strategies must be flexible, sensitive to the cultural beliefs of the family and acceptable to the community where the adolescent resides. The involvement of the parents and extended family is also important because they must act as role models, and provide encouragement and reinforcement of lifestyle changes. As with type 1 diabetes, success is dependent on all family members adopting the same healthy eating habits. The family should be encouraged to reduce the presence of 'junk food' that contains a high percentage of saturated fat, and reduce the intake of 'fast food', prepared food and restaurant prod-

ucts. This may require an exploration of parenting styles and a reduction in pocket money of the child. The youth should be encouraged to increase their intake of fibre, fruits and vegetables. A formal meal plan is seldom useful. Barriers to healthy nutrition for adolescents include the increased cost of healthy choices, reduced satiety with lower calorie food choices, peer pressure, school fundraising activities that use popular fast food selections (eg, pizza, ice cream, hot dogs, pop) and the increased availability of high fat food choices at local restaurants (eg, pan fries, French fries and gravy).

Increasing the physical activity of adolescents is most successfully achieved through *unorganized* community activities, such as walking to school, shopping and community events. Such activities should total at least 150 mins per week. Many northern communities do not have any organized sports activities for adolescent females. Other barriers preventing youth in the north from participating in physical activities include frigid weather, wolves, lack of facilities, lack of adult supervision and leadership, concern for personal safety, and negative peer pressure.

Attention to the psychosocial issues of adolescence is vital. Counselling about the impact of diabetes on their lives is critical for these teens. Many have fatalistic or nihilistic views of diabetes that have been adopted from their parents or extended family. Many believe that there is a supernatural force governing fate. Many are living with or have witnessed the tragic consequences of the complications of diabetes. Many believe that insulin is responsible for the loss of limbs and death associated with diabetes. It may be very difficult for these adolescents to accept that they may have any control over the outcome of their diabetes. Many teens struggle with satisfying the basic needs for personal safety, food, clothing and housing. Many experiment with smoking, drugs, sex and alcohol, which will affect their risk of experiencing complications associated with diabetes. An intensive treatment strategy for these adolescents must include an enhancement of self-esteem and empowerment. For Aboriginal youth with treaty status in Canada, the cost of supplies is not a barrier to treatment because supplies are provided free-of-charge and are readily available.

Natural health products and alternative therapies

The availability and use of natural health products and alternative therapies in North America has grown explosively. Alternative therapies include massage therapy, healing touch, acupuncture, sweat lodges, yoga and herbs. Natural health products include vitamins, trace elements, herbs and traditional medicines. The increased interest in these modalities has resulted in new legislation in Canada to govern the sale of natural health products and alternative therapies (10). For some natural products, it may not be appropriate to conduct clinical trials to define efficacy, especially if the product is prepared for individual consumption by a traditional healer. A safe natural product that increases self-esteem, im-

proves a sense of well-being, helps control weight gain and improves blood glucose control may be an important adjunct to therapy.

PHARMACOLOGICAL THERAPY

In adults with type 2 diabetes, the recommended length of treatment for determining success is three to six months. The Canadian Diabetes Association's clinical practice guidelines recommend starting an oral drug if the fasting blood glucose level is greater than 8 mmol/L after three months of maximal effort on diet and exercise (11). For many adolescents, their families and communities, this is a very short time and doomed to failure because they may not be able to make the required changes in lifestyle that quickly. If there is a slow, consistent improvement in fasting blood glucose levels and hemoglobin A1C, it may be prudent to continue intensive lifestyle and psychosocial counselling for a longer time to capitalize on the initial success and maintain consistent improvement.

Oral drugs

In adults, diet and exercise are successful in only about 20% of patients after six years of therapy (11,12). Ultimately, most adults require pharmacological intervention with oral agents and/or insulin. The United Kingdom Prospective Diabetes Study proved that intensive diabetes management in type 2 diabetes by *whatever single or combination therapeutic regimen* to maintain normal fasting blood glucose levels resulted in a significant reduction in all long term complications of diabetes (13,14).

The long term outcome of therapy in children is unknown, but anecdotal experience suggests that conventional approaches to diet and exercise are successful in only about 30% of children within a few years after diagnosis of diabetes (1,3,6,15). Short term or long term drug therapy may be necessary to control blood glucose levels and prevent microvascular complications. *Unfortunately, none of the oral drugs used have been approved or studied in randomized controlled trials (RCTs) in this age group.*

There are four classifications of oral antihyperglycemic drugs for type 2 diabetes: sulphonylureas, biguanides, alpha-glucosidase inhibitors and thiazolidinediones. Most are given once or twice daily. All of these agents are effective in reducing hemoglobin A1C in adults by 1% to 2%. Many agents are used in combination to achieve an additive effect. They are also used in combination with insulin for increased effect. The therapeutic regimen should be individualized by increasing the dosage of a single agent, or adding a second or third agent every two to three months until the desired therapeutic effect is achieved (11).

The second generation of sulphonylureas (ie, glyburide, glicazide, glimepiride) work primarily by stimulating pancreatic insulin secretion. Stimulation of insulin

secretion also causes the undesirable effects of hypoglycemia and weight gain. Sulphonylurea drugs are common causes of severe hypoglycemia in accidental overdoses in young children and, for this reason, must be stored properly.

The most popular biguanide is metformin, which acts to reduce hepatic glucose production but also has an effect on the insulin receptor and post-receptor function to reduce insulin resistance. It does not cause hypoglycemia or weight gain and has been recommended for obese adults with type 2 diabetes (11, 14). Its most common side effects are self-limited gastrointestinal complaints of diarrhea, nausea and epigastric discomfort in up to 30% of people. This is reduced by the slow upward titration of dosage and by taking the drug with meals. Metformin rarely causes lactic acidosis and is contraindicated in renal or hepatic insufficiency. It must also be withheld for radiographic procedures requiring contrast material (eg, intravenous pyelogram).

Alpha-glucosidase inhibitors (ie, acarbose and miglitol) block the digestion of starch, delay glucose uptake in the gastrointestinal tract and depress the post meal rise in blood glucose. The major side effects are gastrointestinal in nature, with over 50% of adults experiencing flatulence, diarrhea and abdominal cramps. These side effects can be minimized with the slow upward titration of dosage.

The fourth and most recent class of drugs to manage diabetes is the thiazolidinedione group (ie, troglitazone and rosiglitazone), which target insulin resistance and increase insulin sensitivity. There are rare cases of hepatic disease and deaths due to liver failure associated with these drugs. This class of drugs is approved but has not yet been released in Canada.

There are many age-specific barriers to the use of oral drugs by adolescents with type 2 diabetes. These include the lack of symptoms of hyperglycemia, social stigma and denial of illness, socially unacceptable gastrointestinal side effects, the recommended avoidance of alcohol, other risk taking behaviours that interfere with taking pills, and fear of hypoglycemia (with sulphonylureas). Adolescents may not believe that there is a benefit to long term treatment. All of the oral agents are currently contraindicated in pregnancy, and adolescents are a high risk group for pregnancy. Historically, the population requiring these drugs was past reproductive age. Although the teratogenicity of oral agents is controversial (15), there have been no definitive safety studies in pregnancy to address this issue. Thus, contraception is mandatory with oral drug treatment of type 2 diabetes in adolescent females.

Properly designed RCTs are urgently needed to determine optimal dosing and side effects for oral agents used to control type 2 diabetes in children. The number of cases available for RCTs remains relatively small and is geographically isolated across North America, necessitating multicentre long term studies. The industry must be prepared to fund long term studies to assess the impact of oral agents on growth and puberty.

There are many drugs that are used in children without any safety or efficacy data available to assess dosages, pharmacokinetics, drug interactions or the effect of drug use on growth and puberty (16). In most cases, new drugs are not labelled for use in children because adequate studies have not been conducted in children. One of the most significant barriers to studying new drugs in children is the length of time required to assess the impact of drugs on growth and puberty. Other barriers are the lack of understanding about the informed consent process in children, the co-existence of controlled and uncontrolled protocols, the use of short term surrogate outcomes and the belief that large post marketing databases can provide evidence of therapeutic benefit. For at least three decades, the Canadian Paediatric Society has been a strong voice calling for more appropriate and comprehensive drug studies aimed at determining the safety and efficacy of drugs for Canadian children (17). In response to the paucity of drug studies in children, the International Committee on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is developing a framework for conducting clinical research on drug therapy in the paediatric population (18). It is the responsibility of the paediatric community, the pharmaceutical industry and the regulatory agencies to develop strategies to overcome the barriers to properly designed RCTs in drug therapies for children (17,19).

Insulin

Although paediatricians are familiar with the use of insulin in children with type 1 diabetes, its use is not well studied in children with type 2 diabetes. As noted previously, short term insulin therapy after diagnosis may be indicated in some youth with type 2 diabetes. In others, short term insulin therapy may be indicated to improve glycemic control. Insulin has an important role in the treatment of the later stages of type 2 diabetes. As the duration of diabetes increases, the likelihood of the need for insulin increases when failure of the beta cell and persistent insulin resistance cause relative insulin deficiency. For this reason, most adults with type 2 diabetes will eventually need insulin (12). Insulin is often started as a single dose at bedtime, in combination with oral drugs during the day. In adults, insulin regimes may not need to be as complex, insulin dose adjustments are not needed as frequently and hypoglycemia occurs less frequently with insulin therapy in type 1 diabetes. Many adults achieve glycemic targets with bid regimes of 0.5 to 1.0 u/kg/day. Weight gain is an undesirable side effect of insulin therapy in adults with type 2 diabetes. Whether the observations in adults are similar to those in adolescents with type 2 diabetes remains to be studied systematically.

The experience of Manitoba during the past 15 years reveals that few adolescents with type 2 diabetes accept daily insulin therapy. In contrast with adolescents with type 1 diabetes who develop symptoms of ketosis and ke-

toacidosis after 48 to 72 h of insulin omission, youth with type 2 diabetes suffer no consequences from insulin omission. Thus, there is limited incentive to take painful injections. Logistical, cultural and psychosocial barriers are significant in preventing optimal insulin therapy. There may be a perception that insulin is the end-of-the-line therapy based on an adolescent's personal experience with older family members. Weight gain and hypoglycemia are serious side effects of insulin for adolescents. Fortunately, many adolescents have learned from family members that to prevent hypoglycemia, insulin should not be taken with alcohol; however, the use of alcohol remains an important risk for hypoglycemia.

Drugs for obesity

Pharmacotherapy directed at controlling obesity may be a useful adjunct to diet and physical activity in certain situations. With the recent development of safer drugs for obesity, there has been a shift towards the acceptance of pharmacological therapy for morbid obesity in adults. *None of these oral agents have been studied or approved for use in children under 16 years of age.* The new oral agents include sibutramine, an appetite suppressant that inhibits norepinephrine and serotonin reuptake, and orlistat, an inhibitor of pancreatic lipase that reduces fat absorption. Because these two drugs have different modes of action, theoretically they may be used together for added benefit. With the recent international standardization of the definition of obesity by the World Health Organization in children using Body Mass Index percentiles, the paediatric community will welcome RCTs of pharmacological interventions for obesity in children. There may be a benefit to both the primary prevention of type 2 diabetes and the improvement in glycemic control in those with type 2 diabetes.

CONCLUSIONS

The treatment of type 2 diabetes in children represents a unique challenge for paediatricians because of the long experience with this disease in adults but its short history in children. The education and management of diabetes in these children must recognize the unique developmental, emotional and social issues associated with this age group, as well as the cultural, linguistic, geographic and socioeconomic issues associated with this population. With the exception of insulin, the drugs used for adults with type 2 diabetes have not been studied in children. There is an urgent need to design and implement long term, multicentre RCTs of pharmacological therapy in children with type 2 diabetes.

In Aboriginal communities in Canada, there are many exciting primary prevention programs that target and involve all age groups (20). The agents of change associated

with these primary prevention initiatives in Canada will have an important impact on the lives of children with type 2 diabetes because they will foster development of healthier communities.

ACKNOWLEDGEMENTS: This paper represents 15 years of experience working with northern communities and their leaders. The awareness of diabetes in Aboriginal people in Canada has increased recently due in part to the concern of community members for their children and future generations. I am grateful for the privilege of working and struggling with them on this problem. This paper also represents the collective experience of the members of the Manitoba Diabetes Education Resource for Children and Adolescents. I thank them for their commitment, dedication, creativity, flexibility and adaptability in exploring ways of working with these children and adolescents to treat this new disease. There are no books or manuals to guide them.

REFERENCES

- Rosenbloom AL, Joe J, Young RS, Winter WE. Emerging epidemic of type 2 diabetes in youth. *Diabetes Care* 1999;22:345-54.
 - Dean HJ. Diagnostic criteria for non-insulin-dependent diabetes mellitus in youth (NIDDM-Y). *Clin Pediatr* 1998;37:67-71.
 - Dean HJ. NIDDM-Y in First Nation children in Canada. *Clin Pediatr* 1998;37:89-96.
 - Dabelea D, Hanson RL, Bennett PH, Roumain J, Knowler WC, Pettitt DJ. Increasing prevalence of type 2 diabetes in American Indian children. *Diabetologia* 1998;41:904-10.
 - Fagot-Campagna A, Knowler WC, Pettitt DJ. Type 2 diabetes in Indian children: Cardiovascular risk factors at diagnosis and 10 years later. *Diabetes* 1998;47(Suppl 1):A605.
 - Jones KL. Non-insulin-dependent diabetes mellitus in children and adolescents: the therapeutic challenge. *Clin Pediatr* 1998;37:103-10.
 - Venkat Narayan KM, Hoskin M, Kozak D, et al. Randomized clinical trial of lifestyle interventions in Pima Indians: A pilot study. *Diabet Med* 1998;15:66-72.
 - Pinhas-Hamiel O, Dolan LM, Zeitler PS. Diabetic ketoacidosis among obese African-American adolescents with NIDDM. *Diabetes Care* 1997;20:484-6.
 - Anderson KA, Dean HJ. The effect of diet and exercise on a native youth with poorly controlled NIDDM. *Beta Release* 1990;14:105-6.
 - Natural Health Products: A New Vision. Report of the Standing Committee on Health. November 1998. <www.parl.gc.ca>
 - Meltzer S, Leiter L, Daneman D, et al. 1998 Clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. *CMAJ* 1998;159(Suppl 8):S1-29.
 - UK prospective diabetes study Group 16. Overview of six years' therapy of type II diabetes: A progressive disease. *UK Prospective Diabetes Study Group. Diabetes* 1995;44:1249-58.
 - Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *UK Prospective Diabetes Study (UKPDS) Group. Lancet* 1998;352:837-53.
 - Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes. (UKPDS34). *UK Prospective Diabetes Study (UKPDS) Group. Lancet* 1998;352:854-65.
 - Towner D, Kjos SL, Leung B, et al. Congenital malformations in pregnancies complicated by NIDDM. *Diabetes Care* 1995;18:1446-51.
 - Turner S, Longworth A, Nunn AJ, Choonara I. Unlicensed and off label drug use in paediatric wards: prospective study. *BMJ* 1998;316:343-5.
 - Macleod SM. Paediatric pharmacology and toxicology: Drug therapy research for children rather than on children. *Paediatr Child Health* 1998;3:393-4.
 - Topics and Guidelines, Efficacy, #E11. <www.ich.org>
 - Guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations. Committee on Drugs, American Academy of Pediatrics. *Pediatrics* 1995;95:286-94.
 - Macaulay AM, Paradis G, Potvin L, et al. Primary prevention of type 2 diabetes in First Nation: Experiences of the Kahnawake Schools Diabetes Prevention Project. *Can J Diabetes Care* 1998;22:44-9.
-

Type 2 diabetes in children and adolescents

Answer the following questions by circling the letter of the correct answer(s). Answers can be found on page 276.

1. The fundamental treatment of type 2 diabetes in children is:
 - (a) metformin.
 - (b) improved nutrition and intense physical activity.
 - (c) insulin.
 - (d) acarbose.
2. Barriers to nonpharmacological treatment include:
 - (a) lack of motivation due to absence of symptoms.
 - (b) lack of access to fresh, nutritious food.
 - (c) lack of opportunities for participation in physical activity.
 - (d) all of the above.
3. The oral agent that will likely have the best treatment profile in adolescents is metformin because:
 - (a) the majority of affected adolescents are obese.
 - (b) gastrointestinal side effects are self-limiting.
 - (c) it does not cause weight gain or hypoglycemia.
 - (d) all of the above.
4. The use of sulphonylurea agents is limited by side effects that include:
 - (a) liver failure.
 - (b) lactic acidosis.
 - (c) weight gain and hypoglycemia.
 - (d) gastrointestinal complaints.
5. Primary prevention initiatives in communities have an important therapeutic effect on adolescents with type 2 diabetes because:
 - (a) they promote healthy nutrition and physical activity.
 - (b) there is a school curriculum.
 - (c) there is less junk food available.
 - (d) infants and young mothers are targeted.