Cardiovascular and metabolic risk in China: What are the issues and challenges?

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China-Japan Friendship Hospital
Cardiovascular Institute & Fuwai Hospital
Chinese Academy of Medical Science
Diabetes is a leading cause of death. Approximately 5 million deaths were attributable to diabetes in 2015 more than those from HIV/AIDS, tuberculosis, and malaria combined.

In 2010, an estimated 113.9 million adults in China had diabetes.

While excess risk for death among people with diabetes has been well-documented in western populations much less information is available in Asian populations, especially in China.

Update and Next Steps for Real-World Translation of Interventions for Type 2 Diabetes Prevention: Reflections From a Diabetes Care Editors’ Expert Forum Diabetes Care 2016;39:1186–1201
Association Between Diabetes and Cause-Specific Mortality in Rural and Urban Areas of China

Compared with adults non-diabetes, diabetes had a increased risk of all-cause mortality 1,373 vs 646 deaths per 100,000 pys adjusted RR, 2.00 [95%CI, 1.93-2.08]).

It was higher in rural areas than in urban areas
Rural RR, 2.17 [95%CI, 2.07-2.29]
urban RR, 1.83 [95%CI, 1.73-1.94]

Diabetes population’s lifespan is 10 years shorter than NGT — 23-Year follow-up (1986—2009)

For subjects live over 70 yr: DM 56%, NGT 78%
Challenge of Cardiovascular disease in type 2 diabetes
Diabetes was associated with increased mortality from:

- Ischemic heart disease: 3287 deaths; RR, 2.40
- Stroke: 4444 deaths; RR, 1.98
- Chronic liver disease: 481 deaths; RR, 2.32
- Infections: 425 deaths; RR, 2.29
Diabetes and Cause-Specific Mortality In China

Cancer of the liver  (1325 deaths; RR, 1.54)
    pancreas     (  357 deaths; RR, 1.84 )
    Female breast (  217 deaths; RR, 1.84)
Reproductive system ( 210 deaths; RR, 1.81 )

Among diabetes, **10% of all deaths** (16% rural; 4% urban) were due to definite or probable **diabetic ketoacidosis or coma**.
Incidence of CV mortality in DM and NGT population in Daqing
-----China Daqing Diabetes Study (1986-2009)

NDD/NGT HR (95%CI)
Men: 3.5 (2.3-5.3)
Women: 6.9 (3.3-14.2)
糖尿病死亡分布（1986-2009, follow 20000+人年）

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<tr>
<th></th>
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<tr>
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<td>86</td>
<td>17.5 (13.8-21.2)</td>
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<td>CHD</td>
<td>41</td>
<td>8.4 (5.8-10.9)</td>
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<td>Stroke</td>
<td>45</td>
<td>9.2 (6.5-11.8)</td>
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<td>95</td>
<td>19.4(15.5-23.2)</td>
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<td><strong>All-cause</strong></td>
<td>181</td>
<td><strong>36.9 (31.5-42.3)</strong></td>
<td>157</td>
<td><strong>27.1 (22.9-31.4)</strong></td>
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糖尿病与正常人（男+女）CVD千人年死亡率比较（1986-2009）

糖尿病比正常人CVD死亡提前逾10年
China has the world’s largest diabetes population.
China has the world’s largest diabetes population (age adjusted based on 2000 standard population)
IGT without intervention (1986-2006)

- Severe Retinopathy: 17%
- Any death: 32%
- MI or Stroke: 44%
- Progress to Diabetes: 93%
Pre-diabetes is a population with a high risk of CVD. Compared with NGT group, IGT group had 2 folds higher rates of hypertension, obesity and albuminuria.

Minnesota code identified CHD was 9.5 folds higher than NGT
Age-standardized all-cause mortality (per 1000 pysical years)

**IGT group**

| Count | 47/7294 | 15.9 per 1000 pysical years |

**NGT group**

| Count | 26/7066 | 9.3 per 1000 pysical years |

† Rate for normal glucose tolerance (NGT) group is standardized to impaired glucose tolerance (IGT) group
<table>
<thead>
<tr>
<th></th>
<th>心血管病死亡 (%)</th>
<th>癌症死亡 (%)</th>
<th>糖尿病相关死亡 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>正常血糖组</td>
<td>37.62</td>
<td>39.60</td>
<td>2.97</td>
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<tr>
<td>糖尿病前期组</td>
<td>44.65</td>
<td>25.60</td>
<td>9.52</td>
</tr>
<tr>
<td>糖尿病组</td>
<td>51.00</td>
<td>15.06</td>
<td>17.77</td>
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During the 23-year follow-up, 174 (32.1%) died, 15.9/1,000 person-years.

The majority of deaths (74.7%; 130 of 174) occurred after progression to type 2 diabetes.

Age-adjusted death rates:
- 11.1/1,000 person-years (95% CI 8.2–12.0) before
- 19.4/1,000 person-years (95% CI 11.9–23.3) after the development of type 2 diabetes.
Do nothing to prevent diabetes is not acceptable
Prevention of Cardiovascular disease in pre-diabetes
China DaQing Diabetes Prevention Study Design

- 110,600 screened
- 577 Eligible participants randomized
- 530 completed

- Diet (n=130)
- Exercise (n=141)
- D & E (n=126)
- Placebo (n=133)
Interventions

**Diet Group**
Encouraged to follow a Chinese standardized diet
- BMI < 25: 30 kcal / kg/day: reduce alcohol and sugar intake
- BMI >25: reduce calories to reduce weight 0.5-1.0 kg/month

**Exercise Group**
- Increased regular leisure physical exercise

**Diet and Exercise Group**
- Same as Diet and Exercise group
- All of the intervention groups received counseling, weekly for 1 month, monthly for 3 months, once per 3 month for the remainder of the 6 year active intervention.

**Control Group**
- Received standard general health advice.
Results

Following six-years of active intervention, compared with controls, incidence of diabetes was reduced by:

- 31% in the diet group
- 46% in the exercise group
- 42% in the diet & exercise group

The incidence was reduced regardless of initial BMI.

In 1992, all participants were informed of the results of the trial and asked to continue with usual medical care.
Importantly, the effects of life-style modification in reducing T2DM incidence in high-risk individuals, first shown in Da Qing, were later confirmed by other randomized clinical trials— the Finnish DPS (2001), US DPP (2002), Japanese Study (2005), Indian Study (2006).
Some important questions remained

Does the **reduction** in incidence of **diabetes** persist after the intervention is ended, and for how long?

Does life-style intervention of diabetes **ultimately extend to reduce** the risk of **diabetes-related complications** and reduce mortality?
Cumulative incidence of Diabetes (1986-2006)
(G.Li et al, Lancet 2008)

Years of follow up

Percentage (%)

Control
Intervention

Number needed to treat (for 6 years) to prevent a case over 20 years equals 6 people

*1986-1992  Hazard rate ratio  0.49  ( 95% CI  0.33-0.73 )
1986-2006  Hazard rate ratio  0.57  ( 95% CI  0.41-0.81 )
## Effect of Lifestyle Intervention on CVD Mortality (1986-2009)

### All-cause mortality

<table>
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<tr>
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<th>Intervention (N=438)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>53</td>
<td>121</td>
</tr>
<tr>
<td>Incidence/1000/pys (95% CI)</td>
<td>19.9 (14.5-25.2)</td>
<td>14.3 (11.8-16.9)</td>
</tr>
<tr>
<td>Cumulative incidence (%) (95% CI)</td>
<td>38.4 (30.3-46.5)</td>
<td>28.1 (23.9-32.4)</td>
</tr>
<tr>
<td>Hazard rate ratio § (95% CI)</td>
<td>1.00</td>
<td>0.71 (0.51-0.99)</td>
</tr>
</tbody>
</table>

### CVD mortality

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<td>Deaths</td>
<td>27</td>
<td>51</td>
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<tr>
<td>Incidence/1000/pys (95% CI)</td>
<td>10.1 (6.3-14.0)</td>
<td>6.0 (4.4-7.7)</td>
</tr>
<tr>
<td>Cumulative incidence (%) (95% CI)</td>
<td>19.6 (12.9-26.3)</td>
<td>11.9 (8.8-15.0)</td>
</tr>
<tr>
<td>Hazard rate ratio § (95% CI)</td>
<td>1.00</td>
<td>0.59 (0.36-0.96)*</td>
</tr>
</tbody>
</table>

*P values: * <0.05, ** < 0.01. § adjusted for randomization by clinic. pys = person-years. P=0.049 for all-cause mortality, P=0.033 for CVD mortality.
Cumulative incidence of **CVD mortality** over the 23-year follow-up (1986-2009)

HR = 0.59
95% CI (0.36-0.96)
Impacts of *progression to diabetes* on mortality and incidence of CVD event (per 1000 person-years) in Da Qing Study (1986-2009)

<table>
<thead>
<tr>
<th>Variable (n=542)</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>All-cause mortality (174 deaths)</td>
<td></td>
<td></td>
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<tr>
<td>Age (year)</td>
<td>1.09</td>
<td>1.07-1.11</td>
</tr>
<tr>
<td>Sex (male=1)</td>
<td>1.44</td>
<td>0.98-2.10</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>1.006</td>
<td>1.0-1.01</td>
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<tr>
<td>Smoking (yes/no)</td>
<td>1.51</td>
<td>1.09-2.09</td>
</tr>
<tr>
<td>Intervention</td>
<td>0.93</td>
<td>0.67-1.30</td>
</tr>
<tr>
<td>Diabetes status*</td>
<td>1.68</td>
<td>1.16-2.44</td>
</tr>
<tr>
<td>CVD event (213 events)</td>
<td></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>1.06</td>
<td>1.04-1.08</td>
</tr>
<tr>
<td>Sex (male=1)</td>
<td>1.29</td>
<td>0.94-1.78</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>1.007</td>
<td>1.001-1.013</td>
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<tr>
<td>Smoking (yes/no)</td>
<td>1.09</td>
<td>0.81-1.48</td>
</tr>
<tr>
<td>Intervention</td>
<td>0.98</td>
<td>0.72-1.33</td>
</tr>
<tr>
<td>Diabetes status*</td>
<td>2.02</td>
<td>1.43-2.86</td>
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*Diabetes status as time-dependent variable*
Impacts of screen based diabetes and hypertension on fatal and non-fatal CVD events (23 year follow-up of Daqing Diabetes Study 1986-2009)

- NGT: 11.5/1000pys
- DM: 28/1000pys
- HT: 26.2/1000pys
- DM&HT: 41.9/1000pys

FOLLOW-UP YEAR

- DM/NGT HR=2.17
- HT/NGT HR=2.43
- DM&HT/NGT HR=3.49

Age, Sex, smoking adjusted
The results in the Lancet Diabetes & Endocrinology reported by Li and colleagues—which describe the effect of lifestyle intervention on cardiovascular and all-cause mortality—are a real breakthrough, showing that lifestyle intervention can reduce the risk of long term cardiovascular consequences of diabetes.

The lesson from the DaQing Prevention Study is that such long-term studies have scientific value, but the challenge is to match the excellent completeness of follow-up achieved in this study in an equally efficient manner in other trials.

University of Cambridge, Institute of Metabolic Science, Cambridge, UK.
Editorial (The Lancet 2014, June 7)

Back to basics for diabetes

Reliable information is needed to empower people to make informed lifestyle changes and to support wider efforts to reduce obesity and diabetes. Although information is limited, the 23 year follow-up of the Da Qing Diabetes Prevention Study, reported this month in The Lancet Diabetes & Endocrinology, shows that a time-limited diet and exercise intervention in people with impaired glucose tolerance can reduce subsequent diabetes and cardiovascular mortality. Such low-technology interventions have great potential, especially for developing countries in which diabetes is increasing most rapidly. Environment for inaction. Robustly designed, properly funded research is needed to examine nutrition quality and clarify interventions that can be widely adopted to improve long-term public health, bearing in mind that, like Da Qing, benefits may accrue over decades.
23 years Cumulative all-cause mortality according to time to Onset of diabetes (1986-2009)

Among pre-diabetes population, the earlier progression to diabetes, the higher all cause mortality.
Subsequent cumulative incidence of stroke (1993 to 2009) among people with IGT progressed to DM or reversed to NGT in a 6 year trial.

Adjusted cumulative event curve

- NDM vs NGT: HR 1.52, (95% CI 1.02-2.24)
- IGT vs NGT: HR 1.09, (95% CI 0.66-1.82)
Diabetes and pre-diabetes population had significantly higher cardiovascular and metabolic risk in China.

long-term data from major diabetes prevention studies shows that improved long-term lifestyle is achievable, cost-effective and worthwhile clinically.

Translating these benefits to routine community practice will deliver major benefits to public health.

This is a battle we must win.
THANK YOU FOR YOUR ATTENTION

2016.10