Overdiagnosis and the Epidemic of Pre-Diabetes

John S. Yudkin
Emeritus Professor of Medicine,
University College London
TWO MUCH MEDICINE

The epidemic of pre-diabetes: the medicine and the politics

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University of California Health Net members, please click here.

1 in 3 adults in the U.S. has prediabetes. 90% don’t know it.

Find out if you’re one of them. It’s 4 simple questions and only takes a minute.

TAKE THE TEST
You are at **high risk** for prediabetes, according to the CDC.

Anyone 65 or older is considered to be at risk for prediabetes, which is an early stage of type 2 diabetes. It is defined as blood glucose (sugar) that is higher than normal, but not yet at diabetic levels. Without intervention, most people with prediabetes will progress to type 2 diabetes. Fortunately, modest lifestyle changes can address this.

Be a good friend.

Post this quiz so the people you love can find out if they’re at risk. (Your results will never be shared - just the quiz itself).
Outline

• The concept of ‘Intermediate Hyperglycaemia’
  - Predicting future diabetes and CVD
  - Intervention
    - diabetes prevention (or delay)
    - preventing patient-relevant complications

• Using 2hPG, FPG and HbA1c to define risk

• ADA versus The World – the Politics of Pre-Diabetes

• Public Health or the Medical Model
The concept of ‘Intermediate Hyperglycaemia’

- Predicting future diabetes and CVD
‘Intermediate Hyperglycaemia’ Categories

Impaired Glucose Tolerance

– 2hPG 7.8 - 11.1 mmol/l

(NDDG, 1979)
Incident CVD In Subjects With IGT

DECODE Study – 29,714 subjects aged 30-89, mean follow-up 11 years

DECODE Study Group, Diabetes Care 2003
Lifetime Risk of Blindness by Age, HbA1c

Age at diagnosis

Ann Int Med 1997;127:788
The concept of ‘Intermediate Hyperglycaemia’

- Predicting future diabetes and CVD

- Intervention
  - diabetes prevention (or delay)
  - preventing patient-relevant complications
‘Pre-Diabetes’ and Prevention

10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study

Diabetes Prevention Program Research Group*

Figure 3: Cumulative frequency of diabetes

Lancet 2009; 374: 1677–86
Pioglitazone for Diabetes Prevention in Impaired Glucose Tolerance

Ralph A. DeFronzo, M.D., Devjut Tripathy, M.D., Ph.D., Dawn C. Schwenke, Ph.D., MaryAnn Banerji, M.D., George A. Bray, M.D., Thomas A. Buchanan, M.D., Stephen C. Clement, M.D., Robert R. Henry, M.D., Howard N. Hodis, M.D., Abbas E. Kitabchi, M.D., Ph.D., Wendy J. Mack, Ph.D., Sunder Mudaliar, M.D., Robert E. Ratner, M.D., Ken Williams, M.Sc., Frankie B. Stentz, Ph.D., Nicolas Musi, M.D., and Peter D. Reaven, M.D., for the ACT NOW Study

Incident CVD in Subjects With IGT

DECODE Study – 29,714 subjects aged 30-89, mean follow-up 11 years

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Incident CVD In Subjects With IGT

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Incident CVD In Subjects With IGT

DECODE Study – 29,714 subjects aged 30-89, mean follow-up 11 years

DECODE Study Group, Diabetes Care 2003
Impaired glucose tolerance

Is it a risk factor for diabetes or a diagnostic ragbag?

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P O Box 65001,
Dar es Salaam,
Tanzania
‘Intermediate Hyperglycaemia’ Categories

Impaired Glucose Tolerance
(NDDG, 1979)

- 2hPG 7.8 - 11.1 mmol/l

Impaired Fasting Glucose
(ADA 1997, WHO 1999)

- FPG 6.1 - 6.9 mmol/l
Incident CVD In Subjects With IGT and IFG

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‘Intermediate Hyperglycaemia’ Categories

**Impaired Glucose Tolerance**
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**Impaired Fasting Glucose**
(ADA 1997, WHO 1999)

- FPG 6.1 - 6.9 mmol/l

**Impaired Fasting Glucose**
(ADA 2003)

- FPG 5.6 - 6.9 mmol/l
<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Impaired Glucose Tolerance</td>
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<td>(ADA 2003)</td>
<td>(NOT endorsed by WHO in 2006)</td>
</tr>
</tbody>
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‘Intermediate Hyperglycaemia’ Categories

Prevalence

Fasting Plasma Glucose

- 5.6-6.9 mmol/l (37.5%)
- 6.1-6.9 mmol/l (12.5%)

Old Cutpoint
ADA 2003

- Blue bar: 6.1-6.9 mmol/l
- Red bar: 5.6-6.9 mmol/l

Prevalence:
- 5.6-6.9 mmol/l: 37.5%
- 6.1-6.9 mmol/l: 12.5%
‘Intermediate Hyperglycaemia’ – IGT vs IFG

Graphs showing correlation between first and second 2-hour glucose levels and first and second fasting glucose levels.

- First 2-hour glucose vs second 2-hour glucose:
  - Correlation coefficient: $r = 0.89$

- First fasting glucose vs second fasting glucose:
  - Correlation coefficient: $r = 0.92$
‘Intermediate Hyperglycaemia’ – IFG
‘Intermediate Hyperglycaemia’ Categories

HbA1c
‘Intermediate Hyperglycaemia’ Categories

International Expert Committee (2009)
Convened by ADA, with representatives from EASD and IDF

HbA1c $\geq 6.5\%$ = diagnostic criterion for diabetes
‘Intermediate Hyperglycaemia’ Categories

International Expert Committee (2009)
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HbA1c $\geq 6.5\%$ = diagnostic criterion for diabetes

“The categorical clinical states pre-diabetes, IFG, and IGT fail to capture the continuum of risk and will be phased out of use as A1C measurements replace glucose measurements”

Recommended preventive interventions if HbA1c $\geq 6.0\%$ (and maybe below this level if patient demonstrably at high risk)
‘Intermediate Hyperglycaemia’ Categories

**Impaired Glucose Tolerance**
(NDDG, 1979)

- 2hPG 7.8 - 11.1 mmol/l

**Impaired Fasting Glucose**
(ADA 1997, WHO 1999)

- FPG 6.1 - 6.9 mmol/l

**Impaired Fasting Glucose**
(ADA 2003)

- FPG 5.6 - 6.9 mmol/l

**Pre-Diabetes (ADA 2010)**

- 2hPG 7.8 - 11.1 mmol/l **OR**
- FPG 5.6 - 6.9 mmol/l **OR**
- HbA1c 5.7% - 6.4%
‘Intermediate Hyperglycaemia’ Categories

Prevalence

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<tr>
<th>Fasting Plasma Glucose</th>
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<tr>
<td>6.1-6.9mmol/l</td>
<td>12.5%</td>
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<tr>
<td>6.0-6.4%</td>
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<td>5.7-6.4%</td>
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<th>HbA1c</th>
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<td>5.7-6.4%</td>
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<td>5.8%</td>
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(Pre-)Diabetes in China

Original Investigation
Prevalence and Control of Diabetes in Chinese Adults

Yu Xu, PhD; Limin Wang, PhD; Jiang He, MD, PhD; Yufang Bi, MD, PhD; Mian Li, PhD; Tiange Wang, PhD; Linhong Wang, PhD; Yong Jiang, MS; Meng Dai, BS; Jieli Lu, MD, PhD; Min Xu, PhD; Yichong Li, MS; Nan Hu, MS; Jianhong Li, MS; Shengquan Mi, PhD; Chung-Shiuan Chen, MS; Guangwei Li, MD, PhD; Yiming Mu, MD, PhD; Jiajun Zhao, MD, PhD; Lingzhi Kong, MD; Jialun Chen, MD; Shenghan Lai, MD, MPH; Weiqing Wang, MD, PhD; Wenhua Zhao, PhD; Guang Ning, MD, PhD; for the 2010 China Noncommucriable Disease Surveillance Group

JAMA. 2013;310(9):948-958.

Table 3. Estimated Prevalence of Diabetes Among Chinese Adults

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<tr>
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<th>Total Diabetes</th>
<th>Fasting ≥126, 2-Hour ≥200 mg/dL, and/or HbA₁c ≥6.5%</th>
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<tr>
<td>Overall</td>
<td>11.6 (11.3-11.8)</td>
<td>8.1 (7.9-8.3)</td>
<td>3.5 (3.4-3.6)</td>
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Table 4. Estimated Prevalence of Prediabetes Among Chinese Adults

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<tr>
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# Prevalence and Control of Diabetes in Chinese Adults

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In next 10 years, 29% of global growth in diabetes treatment will take place in China

ADA Chief Scientific and Medical Officer:

2009 Expert Committee unanimous – no evidence for category

Centers for Disease Control (DM Division)
- powerful objections
- heavy investment in prevention – by funding DPP
- pressure on ADA to reconsider

ADA Professional Practice Committee (2010)
- reintroduce term ‘pre-diabetes’
- base category on 2hPG or FPG or HbA1c
- reduce HbA1c cutpoint to 5.7%
<table>
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<tr>
<th>Category</th>
<th>Predicts</th>
<th>Effect of lifestyle interventions</th>
<th>Effect of drugs</th>
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<tr>
<td>Impaired Glucose Tolerance (2hPG 7.8mmol/l-11.1mmol/l)</td>
<td>+++</td>
<td>+++ (delays)</td>
<td>+++ (disguises)</td>
<td>+++</td>
<td>+</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td>Impaired Fasting Glucose (6.1mmol/l-6.9mmol/l)</td>
<td>++</td>
<td>?</td>
<td>(+)*</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Expanded Impaired Fasting Glucose (5.6mmol/l-6.9mmol/l)</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Borderline HbA1c (6.0%-6.4%)</td>
<td>++</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>?</td>
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<td>+</td>
<td>?</td>
<td>?</td>
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<td>?</td>
<td>?</td>
</tr>
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<td>Pre-Diabetes</td>
<td>++</td>
<td>?</td>
<td>?</td>
<td>+</td>
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Discussion Points

• Population Health vs Medical Model

• Should people be prescribed lifelong treatments which will provide no individual benefit?

• Is it ethical for a physician to initiate lifelong treatment if (s)he is unaware of its impact on absolute risk reduction / estimated QALY gains?