How complicated is diabetes?

Jonathan Shaw
Diabetic Complications

**Microvascular Complications**
- Diabetic Retinopathy
- Diabetic Nephropathy
- Diabetic Neuropathy

**Macrovascular Complications**
- Stroke
- Heart Disease
- Peripheral Vascular Disease
Diabetic Complications

**Microvascular Complications**
- Diabetic Retinopathy
- Diabetic Nephropathy
- Diabetic Neuropathy

**Macrovascular Complications**
- Stroke
- Heart Disease
- Peripheral Vascular Disease

**Others**
- Fatty liver disease
- Sleep apnoea
- Cancer
- Depression
- Cog dysfunction
- Frailty
Glycaemia and cognition
Risk of incident Alzheimer’s disease associated with diabetes
Crane et al., NEJM 2013

- 2067 Participants mean age 76, followed for 6.8yrs
- 25.4% developed dementia
- Monotonic increase in risk with increase in glucose
Diabetes was associated with disruptions in the white matter network and these network abnormalities were related to slowing of information processing speed. Results were only partially explained by the presence of vascular lesions.

In patients with diabetes, microstructural abnormalities of white matter tracts is related to slowing of information-processing speed.

White matter tracts were reconstructed from each hemisphere based on a standardized atlas (23), the SLF (A), the ILF (B), the UF (C), and the genu and splenium of the media the CC (D).

Reijmer Y D et al. Dia Care 2013;36:137-144
Diabetes and cancer
Changing distribution of causes of death in T2 diabetes from 1997-2009

Median age at death increased from 74 to 80
Median age at CVD death increased from 75 to 82

Harding, Diabetes Care. 2014; 37:2579-86
Association between diabetes and colorectal cancer incidence in case–control and cohort studies.

<table>
<thead>
<tr>
<th>Authors, y (ref. No.)</th>
<th>Study design</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O’Mara et al., 1985 (26)</td>
<td>Case-control</td>
<td>1.16 (0.86-1.57)</td>
</tr>
<tr>
<td>Kune et al., 1988 (27)</td>
<td>Case-control</td>
<td>1.02 (0.62-1.67)</td>
</tr>
<tr>
<td>Le Marchand et al., 1997 (10)</td>
<td>Case-control</td>
<td>1.40 (1.00-2.10)</td>
</tr>
<tr>
<td>La Vecchia et al., 1997 (33)</td>
<td>Case-control</td>
<td>1.30 (1.00-1.60)</td>
</tr>
<tr>
<td>Levi et al., 2002 (13)</td>
<td>Case-control</td>
<td>1.75 (0.95-3.25)</td>
</tr>
<tr>
<td>Yang et al., 2005 (19)</td>
<td>Case-control</td>
<td>1.42 (1.25-1.62)</td>
</tr>
<tr>
<td>Steenland et al., 1995 (22)</td>
<td>Cohort</td>
<td>1.41 (0.79-2.52)</td>
</tr>
<tr>
<td>Will et al., 1998 (20)</td>
<td>Cohort</td>
<td>1.24 (0.87-1.53)</td>
</tr>
<tr>
<td>Hu et al., 1999 (11)</td>
<td>Cohort</td>
<td>1.43 (1.10-1.87)</td>
</tr>
<tr>
<td>Schoen et al., 1999 (24)</td>
<td>Cohort</td>
<td>1.40 (0.80-2.40)</td>
</tr>
<tr>
<td>Nilsen et al., 2001 (14)</td>
<td>Cohort</td>
<td>1.05 (0.50-2.40)</td>
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<tr>
<td>Khaw et al., 2004 (28)</td>
<td>Cohort</td>
<td>2.78 (1.10-7.00)</td>
</tr>
<tr>
<td>Limburg et al., 2005 (9)</td>
<td>Cohort</td>
<td>1.40 (1.10-1.80)</td>
</tr>
<tr>
<td>Jee et al., 2005 (30)</td>
<td>Cohort</td>
<td>1.13 (1.03-1.23)</td>
</tr>
<tr>
<td>Larsson et al., 2005 (31)</td>
<td>Cohort</td>
<td>1.49 (1.14-1.96)</td>
</tr>
</tbody>
</table>

All studies: RR 1.30 (1.20-1.40)
Women 1.33 (1.23-1.44)
Men 1.29 (1.15-1.44)
Cancer risk related to diabetes in adults in Taiwan

*adjusted for age, sex, hypertension, dyslipidemia, and gout

Diabetes and frailty
Diabetes is associated with a 70% increased risk of mobility disability.
Diabetes is associated with an 80% increased risk of disability in activities of daily living

Diabetes is associated with an 80% increased risk of disability in activities of daily living.

What is the mechanism?
Uncertain, but evidence now indicates that there are significant vascular and metabolic factors in osteoarthritis.

Are diabetic complication rates rising or falling?
Improved survival on ESKD: Finland

Falling incidence of proliferative retinopathy in type 1 DM

- **20-yr incidence**
  - 1965-69: 31.2%
  - 1970-74: 30.3%
  - 1975-79: 19.3%
  - 1979-84: 12.5%

**Hovind P et al. Dia Care 2003;26:1258-1264**
Falling incidence of proliferative retinopathy in type 1 DM

Later cohorts
- BP Rx started earlier
- BP lower
- HbA1c lower
- Fewer smokers

Hovind P et al. Dia Care 2003;26:1258-1264

Percent reductions
- AMI: 68%
- Stroke: 53%
- Amputation: 51%
- ESRD: 28%

Gregg. NEJM 2014; 370:1514-23
Trends in amputation rates

England – national LEA incidence

USA veterans – risk of LEA

Vamos E P et al. Dia Care 2010;33:2592-2597

Major variation in lower limb amputation rates in people with DM across USA and England

USA
5-fold variation in LEA rates

England
10-fold variation in LEA rates

Holman. *Diabetologia* 2012. DOI 10.1007/s00125-012-2468-6
Summary

- Increasing number of complications of diabetes
  - Not clearly micro- or macro-vascular
  - Excess risks more moderate than for classical complications
- Progress in reducing complication rates is starting to occur
- Geographic variability in outcomes remains a significant problem