Supporting people with diabetes and severe mental illness in primary care and the community

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I have received fees for lecturing, consultancy work or attendance at conferences from the following companies: Astra Zeneca, Boehringer Ingelheim, Eli Lilly, Janssen, Lundbeck, Menarini, Mylan, NAPP, Novo Nordisk, Novartis, Otsuka, Sanofi.
The greatest mistake in the treatment of disease is that there are physicians for the body and physicians for the soul, although the two cannot be separated.

Plato circa 370 BC
Diabetes

- Diabetes-related distress
- Depression
- Severe Mental Illness
- Anxiety
- Eating disorders
- Dementia
- Adjustment disorders
- Stigma & discrimination
- Phobia
Overview

• Epidemiology of diabetes in people with severe mental illness

• Why is diabetes more common in people with severe mental illness

• Clinical implications
Prevalence of Diabetes

- Meta-analysis of 41 studies including 161,886 people with severe mental illness

- Overall prevalence was 9.0% (95% CI 7.3–11.1%)

- Risk of diabetes in people with multiple episodes of psychosis was doubled (OR 1.99; 95% CI 1.55–2.54)

- No increase risk of diabetes in first episode psychosis or treatment naive individuals


Diabetes & Schizophrenia

Consequences of diabetes in people with severe mental illness

- 74% more likely to develop acute complications associated with diabetes
- More likely to develop chronic microvascular complications
- 2-3 more likely to develop cardiovascular disease
- 6.14x more likely to die from DM

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Severe mental illness

Common Antecedents

- Genetics
- Fetal Development
- Inflammation
- Neuro-endocrine
- Poor Diet
- Poverty & Deprivation

Severe mental illness

Poor Diet

Physical inactivity

Antipsychotics

Smoking

Obesity

Type 2 diabetes

Person with severe mental illness

- Low physical activity
- Low birth weight
- Social environment
- Genetic polymorphisms

Dysfunctional reward mechanisms

Poor food choices

Obesity

Severe mental illness
- Hypercortisolaemia
- Low IGF-I

Antipsychotics
- Appetite
- Basal metabolic rate (?)
- Sedation
- Altered physical activity

Holt and Peveler Diab Obes Metab 2009 Jul;11(7):665-79
Mean Change in Weight With Antipsychotics

- 4-6 week pooled data (Marder SR, Schizophr Res 2003;61:123-36.). †Extrapolated from 6-week data.
Head-to-head comparisons of effect of second generation antipsychotics on glucose

Comparator Antipsychotic

- Ziprasidone*
- Risperidone
- Quetiapine
- Clozapine
- Aripiprazole
- Amisulpride
- Sertindole

Mean difference in glucose (mg/dL)

Number of trials
- 4
- 9
- 4
- 3
- 3
- 2

Number of patients
- 420
- 1303
- 986
- 89
- 1487
- 406

*Ziprasidone is not licensed for use in the UK

Please refer to product SmPC for complete information on prescribing and adverse events

Possible effects of antipsychotics on β-cell function

Direct toxic effect

Antipsychotics may increase basal insulin secretion by blocking \( \alpha_2 \) receptor

Antipsychotics may blunt glucose stimulated insulin release by blocking the dopamine \( D_2 \) receptor

Antipsychotics may decrease pancreatic β-cell responsiveness to blood glucose by blocking \( 5\text{-HT}_{1a} \) receptor

Antipsychotics may impair cholinergic-stimulated pancreatic insulin secretion by blocking M3 muscarinic receptor

Hieronymus Bosch, Curing Folly: removing the stone of madness, c.1475-1480

Benjamin Rush's Tranquilizer

Number of psychiatric hospital beds
England 1900 - 2000
Overview

- Epidemiology of diabetes in people with severe mental illness
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- Clinical implications
Overview

- Epidemiology of diabetes in people with severe mental illness
- Why is diabetes more common in people with severe mental illness
- Clinical implications
  - Prevention of diabetes
Meta-analysis of effectiveness of weight-management interventions

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.59.1 Prevention trials</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alvarez-Jiménez 2006</td>
<td>4.1</td>
<td>3.99</td>
<td>28</td>
<td>6.98</td>
<td>4.5</td>
<td>33</td>
<td>9.6%</td>
<td>-2.88 [-5.01, -0.75]</td>
<td></td>
</tr>
<tr>
<td>Cordes et al 2011</td>
<td>3.4</td>
<td>4.2</td>
<td>13</td>
<td>4.5</td>
<td>6.1</td>
<td>18</td>
<td>4.8%</td>
<td>-1.10 [-4.73, 2.53]</td>
<td></td>
</tr>
<tr>
<td>Evans 2005</td>
<td>2</td>
<td>3.6</td>
<td>23</td>
<td>6</td>
<td>2.6</td>
<td>11</td>
<td>9.7%</td>
<td>-4.00 [-6.43, -1.87]</td>
<td></td>
</tr>
<tr>
<td>Littrell 2003</td>
<td>0.81</td>
<td>8.97</td>
<td>35</td>
<td>7.17</td>
<td>9.16</td>
<td>35</td>
<td>3.8%</td>
<td>-6.36 [-10.61, -2.11]</td>
<td></td>
</tr>
</tbody>
</table>

Majority of these trials were of short duration, most lasting 12-16 weeks, with small participant numbers (median 53, range 15-110)
People with psychosis or schizophrenia, especially those taking antipsychotics, should be offered a combined programme of healthy eating and physical activity by their mental healthcare provider....
<table>
<thead>
<tr>
<th>Change in weight (kg)</th>
<th>Intervention (N=207)</th>
<th>Control (N=205)</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>-0.2 (4.4)</td>
<td>0.4 (4.7)</td>
<td>-0.58 (-1.48, 0.32)</td>
</tr>
<tr>
<td>12 months</td>
<td>-0.5 (7.9)</td>
<td>-0.5 (8.3)</td>
<td>0.04 (-1.60, 1.67)</td>
</tr>
</tbody>
</table>
Overview

• Epidemiology of diabetes in people with severe mental illness

• Why is diabetes more common in people with severe mental illness

• Clinical implications
  – Screening for diabetes
Recommended physical health screening

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>Annually</th>
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</thead>
<tbody>
<tr>
<td>Medical History</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Height</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>✓</td>
<td>Every visit during 1&lt;sup&gt;st&lt;/sup&gt; 6-8 weeks of treatment. At least quarterly thereafter</td>
<td>✓</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Glucose*</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HbA&lt;sub&gt;1c&lt;/sub&gt;</td>
<td>✓</td>
<td>(✓)</td>
<td>✓</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ECG</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*Either fasting or random. oGTT only rarely indicated
Beware HbA<sub>1c</sub> may be normal if glucose is changing rapidly

Always refer to individual product for complete monitoring information
The effect of the ADA and FDA guidance

Percentage of patients receiving glucose screening

ADA/APA Consensus Statement

FDA warning letter/campaign

- Any
- Baseline

2001  2002  2003  2004

The effect of the ADA and FDA guidance

Percentage of patients receiving glucose screening

ADA/APA Consensus Statement

FDA warning letter/campaign

- Any
- Baseline

Barriers to screening

- Lack of clarity about whose responsibility it is
- Lack of understanding about what should be measured and when
- Lack of confidence in interpreting results
- Lack of access to necessary equipment

Overview

• Epidemiology of diabetes in people with severe mental illness

• Why is diabetes more common in people with severe mental illness

• Clinical implications
  – Management of diabetes
Management of diabetes

• Diabetes is a complex disease to manage
  – Medication
  – Life-style change
  – Empowerment of the patient
• Requires management by a multi-disciplinary team
  – Diabetes team
  – Psychiatric team
• Importance of treating the mental state
Should we stop the antipsychotic?

Role of antipsychotic?

Duration of treatment?

Other risk factors?

Risk of relapse?

Benefits of treatment
Drug treatments for type 2 diabetes

DPP-4 inhibitors
GLP-1 agonists

Incretins
Pancreas
Sulfonylureas meglitinides

Alpha-glucosidase inhibitors

Intestine
Liver
Muscle
Kidney
Adipose tissue

Blood glucose-lowering
Lifestyle diet, exercise

Insulin
Metformin
Glitazones
SGLT2 inhibitors

DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose co-transporter 2

Overview

• Epidemiology of diabetes in people with severe mental illness

• Why is diabetes more common in people with severe mental illness

• Clinical implications
  – Organisation of diabetes services
LES PASSIONS DE L’AME.
PAR RENÉ DES CÉRTES.

A PARIS.
Chez Henry Le Gras, au troisième Pilier de la grande Salle du Palais, à l’ourannée.
M. DC. XEX.
 Avec Privilege Du Roy.
Over-shadowing

HCPs focus solely on their mental disorder and fail to take note of physical health needs.

Less likely to be examined for eye or foot complications
  – Despite more clinic visits

Less likely to be screened for HbA$_{1c}$ or cholesterol

Received less education

Less likely to receive a statin
Summary

• Severe mental illness is associated with a 2-3 fold increase in the prevalence of T2DM
  – The mechanisms underlying the increase are multifactorial

• Individualised lifestyle and treatment is needed to reduce the risk of diabetes in people with severe mental illness

• Treatment of DM should follow standard treatment algorithms

• The management of DM in someone with DM and severe mental illness requires a multidisciplinary approach
Any questions?

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