The association between obesity, cognitive decline and dementia in mid-life and late-life

Professor Kaarin Anstey
Centre for Research on Ageing, Health and Wellbeing

What is dementia?

Dementia is a **SYNDROME**, usually progressive and irreversible.

A syndrome is a pattern of symptoms that may be caused by many different illnesses.

The dementia syndrome has 3 key features:

1. Is acquired
2. Is persistent
3. Involves multiple impairments of intellectual functioning

Main causes of dementia in Australia:

*Alzheimer’s disease, Vascular Dementia*
Dementia is 2nd leading cause of disease burden
Prevalence to increase four-fold from 245,400 in 2009 to 1.13 million in 2050 (Access Economics, 2009)
By 2016, its disability burden will be greater than any disease in Australia
US estimates suggest 20% of adults over 70yrs suffer from significant cognitive impairment
Midlife Cardiovascular risk factors increase risk of late-life dementia in Alzheimer’s and Vascular dementia.
Background

- There is no cure for dementia so risk reduction is essential
- Internationally, obesity is increasing in young adults and middle-aged adults
- Complex associations between bodyweight, adiposity, BMI and cognition and dementia
- Evidence now strongly suggests links mid-life obesity to increased risk of late-life dementia
Bodyweight and dementia

- Excess weight → insulin resistance, hypertension and changes in coronary arteries leading to an increase in risk for cardiovascular disease
- Cardiovascular disease is a risk factor for dementia
- BUT body fat also contains leptin and estrogen which are potentially neuroprotective
- Some studies show high BMI increases risk of dementia
- Some studies show higher BMI in late life is protective against dementia
- Depends on age, distribution of body fat, body composition
Systematic review BMI & dementia - aims

- To synthesise all available high quality data on BMI and risk of dementia in late life
- To evaluate whether BMI in mid-life and BMI in late-life have similar risks for dementia
- To compare findings with other published reviews of BMI and dementia
- To draw inferences from the study for population health strategies to reduce dementia risk
Search Terms


**Dementia and cognition terms** included: Cognit*, Memory, Attention, Reaction time, Speed of processing, Processing speed, Crystallized ability, Crystallized intelligence, Fluid ability, Fluid intelligence, General mental ability, GMA, Intelligence, Executive function, Neuropsychological testing, Mini mental stat* exam* , MMSE, Dementia, Alzheimer (auto explode), Mild cognitive impairment, MCI.
Inclusion criteria

- **Quality had to be**: equal or better than the Oxford Centre for Evidence-Based Medicine Level of Evidence 1B
- **Studies design had to be**: prospective, longitudinal, population based studies with a minimum follow up period of one year.
- **Exposure**: BMI or waist circumference at baseline or during a follow-up period that preceded the final follow-up examination.
- **Outcome**: dementia (research criteria) or cognitive decline. Dementia categories were Alzheimer’s Disease, Vascular Dementia, Any Dementia.
Exclusion criteria

- Studies not screening for dementia at baseline
- Cross-sectional
- Experimental
- Used clinical sample or sample of relatives
- Low quality
- Not meeting inclusion criteria
Studies included

> 90,000 abstracts identified in search, 309 articles obtained after screening abstracts, 26 studies met criteria, 17 compatible for meta-analyses

**Alzheimer's disease**
- \( n = 15256 \) were assessed in mid-life
- \( n = 13166 \) were assessed in late-life

**Vascular dementia**
- \( n = 5299 \) were assessed in late life

**Any dementia**
- \( n = 20476 \) assessed in mid-life
- \( n = 12792 \) assessed in late-life
BMI categories

World Health Organization Categories for Body Mass Index

- Underweight $< 18.5$
- Normal weight $\geq 18.5 < 25$
- Overweight $\geq 25 < 30$
- Obese $\geq 30$
Results: Low BMI in mid-life increases risk of Alzheimer's disease

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>log(Low weight) (SE)</th>
<th>95% CI</th>
<th>Weight</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitzpatrick</td>
<td>0.3852 (0.3788)</td>
<td></td>
<td>28.28</td>
<td>1.47 [0.70, 3.09]</td>
</tr>
<tr>
<td>Whitmer</td>
<td>0.0676 (0.3859)</td>
<td></td>
<td>27.25</td>
<td>1.07 [0.50, 2.28]</td>
</tr>
<tr>
<td>Beydoun</td>
<td>1.2325 (0.3021)</td>
<td></td>
<td>44.47</td>
<td>3.43 [1.90, 6.20]</td>
</tr>
</tbody>
</table>

Total (95% CI)
Test for heterogeneity: Chi^2 = 6.47, df = 2 (P = 0.04), I^2 = 69.1%
Test for overall effect: Z = 3.35 (P = 0.0008)
Results: Overweight BMI in midlife increases risk of AD and dementia

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>log(Overweight) (SE)</th>
<th>Overweight (fixed) 95% CI</th>
<th>Weight %</th>
<th>Overweight (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitzpatrick</td>
<td>0.0392 (0.1751)</td>
<td></td>
<td>14.63</td>
<td>1.04 [0.74, 1.47]</td>
</tr>
<tr>
<td>Vihlmier</td>
<td>0.7376 (0.1098)</td>
<td></td>
<td>37.20</td>
<td>2.09 [1.69, 2.59]</td>
</tr>
<tr>
<td>Beydoun</td>
<td>0.0487 (0.0965)</td>
<td></td>
<td>48.17</td>
<td>1.05 [0.87, 1.27]</td>
</tr>
</tbody>
</table>

Total (95% CI)

Test for heterogeneity: Chi² = 24.88, df = 2 (P < 0.00001), I² = 52.0%

Test for overall effect: Z = 4.53 (P < 0.00001)
Results: Obese BMI mid-life increases risk of AD and dementia

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>log[obesity] (SE)</th>
<th>obesity (fixed) 95% CI</th>
<th>Weight %</th>
<th>obesity (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitzpatrick</td>
<td>0.2231 (0.2673)</td>
<td>22.53</td>
<td>1.25 [0.74, 2.11]</td>
<td></td>
</tr>
<tr>
<td>Whitmer</td>
<td>1.1314 (0.1768)</td>
<td>51.50</td>
<td>3.10 [2.19, 4.38]</td>
<td></td>
</tr>
<tr>
<td>Beydloun</td>
<td>0.3074 (0.2490)</td>
<td>25.97</td>
<td>1.36 [0.83, 2.22]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>100.00</td>
<td>2.04 [1.59, 2.62]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 11.61, df = 2 (P = 0.003), I² = 82.8%
Test for overall effect: Z = 5.62 (P < 0.00001)
Results: BMI in late-life continuous and AD?

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>log[Relative Risk] (SE)</th>
<th>Relative Risk (fixed)</th>
<th>Weight</th>
<th>Relative Risk (fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>95% CI</td>
<td></td>
<td>95% CI</td>
</tr>
<tr>
<td>Yoshitake</td>
<td>-0.2876 (0.1647)</td>
<td></td>
<td>0.76</td>
<td>0.75 [0.54, 1.04]</td>
</tr>
<tr>
<td>Borenstein</td>
<td>0.0582 (0.0838)</td>
<td></td>
<td>2.92</td>
<td>1.06 [0.90, 1.25]</td>
</tr>
<tr>
<td>Gustafson</td>
<td>0.2620 (0.0372)</td>
<td></td>
<td>14.84</td>
<td>1.30 [1.21, 1.40]</td>
</tr>
<tr>
<td>Buchman</td>
<td>-0.0576 (0.0197)</td>
<td></td>
<td>52.90</td>
<td>0.94 [0.91, 0.98]</td>
</tr>
<tr>
<td>Luschinger</td>
<td>-0.1053 (0.0268)</td>
<td></td>
<td>28.58</td>
<td>0.90 [0.85, 0.95]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>100.00</td>
<td>0.98</td>
<td>[0.95, 1.01]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 74.73, df = 4 (P < 0.00001), I² = 94.6%
Test for overall effect: Z = 1.55 (P = 0.12)

Note: Weight loss precedes AD by about 5-6 years
Summary and conclusion of review

- Mid-life low and high BMI are associated with an increased risk of AD and Any dementia in late life. This finding appears relatively robust.
- The mechanism for low BMI may be different than that of high BMI.
- The findings for late-life BMI are not robust because of the short follow-up periods of studies, selection effects in studies of older adults, and lack of co-morbid health data.
Abdominal fat a risk in normal BMI women

Women’s Health Initiative Study
Aged 65-80 (n = 7163)
Examined BMI, waist to hip ratio, 4-5 yrs follow up
Abdominal obesity associated with dementia, even in normal weight women

Figure 1. Hazard ratio for probable dementia with covariate adjustment. *No cases of probable dementia in 41 in this cell. WHR = waist-hip ratio.
Weight loss and cognitive function

Lo et al., 2011, Int. J. Geriatric Psychiatry.
Australian Study: Women aged 40-79 (n = 334), follow up 7.45 years

Mixed results for mid-life weight loss and cognition. No association with change in cognition. Weight loss associated with higher scores on visual memory at follow-up

Inconclusive results → need systematic review
Overall benefit of weight loss found for measures of executive function

Mixed results for memory

Studies had mixed age-range

Assessments mostly taken immediately after weight loss
Dementia prevalence according to obesity

Summary and conclusion

Obesity in young and middle-aged adults will lead to expected increase in dementia rates.

Midlife abdominal obesity and associated inflammation seem most important.

Late-life more complicated results; careful interpretation required.

Population health approaches to obesity epidemic need to acknowledge the long term impacts on dementia, and short term impact on cognitive function.
Acknowledgements

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Reference