Healthy minds for Future Generations
Promoting Dementia Risk Reduction

Predictors of disease, dementia and ‘well being’ in Caerphilly

John Gallacher and Tony Bayer
Janet Pickering and Peter Elwood

Division of Population Medicine, Cardiff University
All Nations Centre, Cardiff. 14th December 2017
Predictors of disease, dementia and ‘well being’ in the Caerphilly Cohort Study

John Gallacher

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OF COGNITIVE HEALTH
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DEMENTIAS PLATFORM UK;

Janet Pickering Statistician

Peter Elwood
Division of Population Medicine,
Cardiff University
All Nations Centre, Cardiff
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Tony Bayer

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OF GERIATRIC MEDICINE
CARDIFF UNIVERSITY
Predictors of disease, dementia and ‘well being’ in the Caerphilly Cohort Study
THE 35-year CAERPHILLY PROSPECTIVE STUDY 1979 - 89

2,500 men aged 45-59 yrs: 90% of men of that age within Caerphilly
Questioned and examined every five years

Extensive data collected on possible predictive factors at baseline

- Social, family, occupational details; psychosocial items, leisure activities, anxiety, depression, anger and other psychosocial factors
- BP, ECG, extensive haematological and biochemical factors
- Blood, serum and tissue samples stored

Clinical outcomes up to 35 years later

- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia; aspects of ‘wellbeing’
- wellbeing: self-perceptions of health, fulfilment, satisfaction etc
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia
- wellbeing: self-perceptions of health, fulfilment, satisfaction etc.
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
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Predictive factors 20-30 years previously
- Social factors and contacts: marriage, family size, social class etc.
- Lifestyle: smoking, exercise, diet, BMI, alcohol
- Baseline mood: GHQ, depression, anxiety
- Auditory Threshold
- Disturbed sleep:
- Leisure and social activities: ‘intellectual’, physical, social
- Vascular disease:
  - ‘Sticky blood’:
  - inflammatory markers
- Head injury
- proximity of green places
Outcomes at age 75-89
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- Social factors and contacts: marriage, family size, social class etc.
- Lifestyle: Non-smoking
- Baseline mood: GHQ, depression, anxiety
- Auditory threshold
- Disturbed sleep: A ‘healthy’ diet
- Leisure and activity
- Vascular disease: Regular physical exercise
- ‘Sticky blood’: Maintenance of a low BMI
- Inflammatory markers
- Head injury
- Green places
- Non-smoking
- Maintenance of a low BMI
- Regular physical exercise
- A ‘healthy’ diet
- A low alcohol intake
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| An ‘Unhealthy’ lifestyle |
| None or only one behaviour |
| A ‘Healthy’ lifestyle |
| Four or five of the behaviours |
### Predictors of disease in the Caerphilly Cohort Study

#### Reductions in chronic diseases

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**Significance of trend**

- Diabetes: 0.001
- Vascular disease: 0.0005
- Cancer: 0.88
- Cognitive decline: 0.001
- Dementia: 0.006

All relationships adjusted for age, social class and other confounding factors.

---

Healthy Lifestyles Reduce the Incidence of Chronic Diseases and Dementia: Evidence from the Caerphilly Cohort Study. Elwood, Galante, Pickering, Palmer, Bayer, Ben Shlomo, Longley, Gallacher. 2013. [https://doi.org/10.1371/journal.pone.0081877](https://doi.org/10.1371/journal.pone.0081877)
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Predictors of disease in the Caerphilly Cohort Study

### Reductions

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### OTHER BENEFITS OF A HEALTHY LIFESTYLE:

- **Delays in the onset of disease**
  - *vascular disease events delayed by an average of 13 years*
  - *death delayed by an average of 6 years*

- **More men retire disease free**
  - *10% of subjects who had neglected healthy living*
  - *23% of those who had followed a healthy lifestyle*

Healthy Lifestyles Reduce the Incidence of Chronic Diseases and Dementia: Evidence from the Caerphilly Cohort Study. Elwood, Galante, Pickering, Palmer, Bayer, Ben Shlomo, Longley, Gallacher. 2013. [https://doi.org/10.1371/journal.pone.0081877](https://doi.org/10.1371/journal.pone.0081877)
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**OTHER BENEFITS OF A HEALTHY LIFESTYLE:**

Disease burden in the community reduced

- *if the subjects in the Caerphilly cohort had each been urged to take up one additional healthy behaviour.... and If only half had done so, there would have been, over the next 30 years.....*

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Disease burden in the community reduced

- *if the subjects in the Caerphilly cohort had each been urged to take up one additional healthy behaviour.... and if only half had done so, there would have been, over the next 30 years.....*

- **12% less diabetes**
- **6% less vascular disease**
- **13% less dementia**

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Predictors of disease in the Caerphilly Cohort Study

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<tr>
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*Is this just the performance of a few behaviours.....or is it a ‘marker’ for a type of person?.....is there a ‘Glasgow’ effect’?*

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### Healthy living, disease and social class

#### Reductions during 35-year follow-up

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**REDUCTIONS by a ‘HEALTHY’ LIFESTYLE**

*All estimates adjusted for age*
## Healthy living, disease and social class

### Reducing trends during 35-year follow-up

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Data from the Caerphilly cohort are available.
Data for cancer have been derived from 1/3 Million subjects and 14,285 cancers in UK Biobank.
See Elwood et al: Healthy living and cancer: evidence from Biobank in eCancer
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**Other benefits of a healthy lifestyle:**

- Dementia delayed by an average of 6 years
- Disease burden in the community reduced
  - If the subjects in the Caerphilly cohort had each been urged to take up one additional healthy behaviour.... and if only half had done so, there would have been, over the next 30 years.....

13% less dementia
## Healthy living, dementia and social class

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<td>Incidence</td>
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All results adjusted for age and for base-line NART
### Dementia, healthy living and social class

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Predictors of dementia in the Caerphilly Cohort Study

Chronic disease and Dementia 15-20 years later

- **diabetes** 13.6% vs 9.1% in subjects with no diabetes
- **vascular disease** 17.0% vs 7.5% in subjects with no vasc. disease
- **hypertension** 13.6% vs 7.8% in normotensive subjects

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1. The risk of dementia is increased by about 50% in men with diabetes
2. Almost 70% of new diabetes is attributable to overweight
3. In diabetes, good control of blood glucose reduces the risk of cognitive loss
4. Primary care-led intensive weight management led to remission in 50% of patients

References:
3. Primary care-led weight management for remission of Type 2 diabetes Lancet Dec 5.2017
Auditory threshold at baseline and dementia 15-20 years later

Baseline auditory threshold assessed at 4 frequencies, twice at a 10 year interval.

Risk of dementia in men with baseline auditory threshold above median:

OR 2.67 (1.38, 5.18) after adjustments for possible confounding

Further analyses suggested that the relationship was for non-vascular dementia OR 2.23 (1.04, 4.77)
Disturbed sleep at baseline and dementia 15-20 years later

20% of the men reported ‘disturbed’ sleep at base-line

OR for vascular dementia 2.04 (1.05, 3.98)

30% complained of ‘severe’ daytime sleepiness at base-line

OR for vascular dementia 4.4 (2.05, 9.61)

No relationships detected with non-vascular dementia

Blood rheology, cognitive loss and dementia 15-20 years later

Haematocrit: sig. reduction in cognitive function at lowest levels $p<0.05$
Plasma viscosity: sig reduction at lowest levels $p<0.05$

Cognitive function and blood rheology: results from the Caerphilly cohort of older men.
Haemostatic and inflammatory indices and dementia

On the basis of an analysis of 15 haemostatic tests:

‘... the coagulation pathways of clotting activity..... increase the risk of vascular dementia......’

On the basis of an analysis of six inflammatory tests:

No significant association with inflammatory markers


Predictors of dementia in the Caerphilly Cohort Study

Haemostatic and inflammatory indices and dementia

On the basis of an analysis of 15 haemostatic tests:

‘... the coagulation pathways of clotting activity... increase the risk of vascular dementia... consistent with a microinfarct model of vascular dementia.'

On the basis of an analysis of six inflammatory tests:

No significant association with inflammatory markers.

‘Sticky blood’ and dementia: ‘...a testable hypothesis!’

Gordon Lowe, Haematologist, University of Glasgow


Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia
- ‘wellbeing’:

Predictors of wellbeing in the Caerphilly Cohort Study
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
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- wellbeing:

‘Wellbeing of Future Generations (Wales) Act 2015’
- ‘prosperous and innovative’, ‘fair share of natural resources’, ‘communities safe, cohesive and resilient’, ‘people participate in our shared culture, with a thriving living Welsh language’,
- ‘people healthier’ and ‘more equal’
Outcomes at age 75-89
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- wellbeing:

Older People’s Commissioner for Wales
‘Wellbeing indicators for older people’

1. **What is well being?**
   - Feel safe, listened to, valued and respected
   - Able to get the help they need, when and in a way they want it
   - Live in a place that suits them and their lives
   - Are able to do the things that matter to them
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- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia
- wellbeing: self-perception of health, fulfilment, satisfaction etc.

There is a large psychological literature....

'WELLBEING'

- general health
  - GHQ, ADL
- cognitive function
  - AH4, MMSE
- social support
  - Diener et al 1985
- self esteem
  - Kupens et al 2008
- satisfaction with life
  - Diener et al 1985
- mood/affect
  - anxiety/depression etc
- inequalities
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia

- wellbeing: self-perception of health, fulfilment, satisfaction etc.

’The good life: from Socrates to Surbiton’
Gallacher et al. Age and Ageing and Older Adults 2011:12:19-27
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
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’The good life: from Socrates to Surbiton’ Gallacher et al.

Structural Equation Monitoring
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia
- wellbeing: self-perceptions of health, fulfilment, satisfaction etc.

In Phase II: Psychosocial factors and leisure activities recorded as possible ‘predictors’

in Phase V: Perceptions of health, activity and psychosocial factors examined as ‘outcomes’
Predictors of wellbeing in the Caerphilly Cohort Study

‘WELLBEING’

- Health
  - GHQ, ADL
- Social support
  - Brown et al 2003
- Self esteem
  - Diener et al 1985
- Satisfaction with life
  - Diener et al 1985
- Positive attitudes
  - Kuppens et al 2008
- Affect
  - Anxiety, depression

Predictive factors 20-30 years previously

- Social factors and contacts: marriage, family size, social class etc.
- Lifestyle
  - More than just having followed five behaviours!
  - Baseline mood: GHQ, depression, anxiety
  - Auditory Threshold
  - Disturbed sleep:
  - Leisure and social activities: ‘intellectual’, physical, social
  - Vascular disease:
  - ‘Sticky blood’:
  - Inflammatory markers
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia
- wellbeing: self perception of health, satisfaction, self-esteem, social support….

Predictors of wellbeing in the Caerphilly Cohort Study

Health at age 75-89 years and prior lifestyle  GHQ and ADL

Subjects own estimate of general health
- ‘Unhealthy’ lifestyle  53% judged themselves to be in ‘good health’
- ‘Healthy’ lifestyle  89% judged themselves to be in ‘good health’  P<000.5
fewer claimed problems with activities of daily living
fewer claimed anxiety or depression
Outcomes at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia

- wellbeing: self perception of satisfaction, self-esteem, social support

Satisfaction with life at age 75-89 and Lifestyle 20 years earlier

- Unhealthy ‘satisfaction with life’ score 26
- Healthy ‘satisfaction with life’ score 28

P<0.06
Predictors of wellbeing in the Caerphilly Cohort Study

**Outcomes** at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia
- **wellbeing**: self perception of satisfaction, self-esteem, social support

**Self-efficacy** at 75-89 years and **Lifestyle** and 15-20 years earlier

<table>
<thead>
<tr>
<th>Score</th>
<th>‘self-efficacy’ score</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Unhealthy</td>
<td>24.3</td>
<td></td>
</tr>
<tr>
<td>Healthy</td>
<td>25.6</td>
<td>&lt;0.05</td>
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</table>
**Outcomes** at age 75-89
- diabetes, vascular disease, cancer and all-cause death
- cognitive decline and dementia

- **wellbeing**: self perception of satisfaction, self-esteem, social support

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**Lifestyle and positive attitudes** 15-20 years later  
*Kuppens et al 2008*

<table>
<thead>
<tr>
<th></th>
<th>‘interested’</th>
<th>‘enthusiastic’</th>
<th>‘useful’</th>
<th>‘capable’</th>
<th>important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unhealthy</td>
<td>60%</td>
<td>38%</td>
<td>57%</td>
<td>57%</td>
<td>72%</td>
</tr>
<tr>
<td>Healthy</td>
<td>85%</td>
<td>62%</td>
<td>85%</td>
<td>62%</td>
<td>78%</td>
</tr>
</tbody>
</table>

P values:
- P<0.0005
- P<0.0005
- P<0.0005
- P<0.0005
- P<0.23
BETTER THAN ANY PILL...

and no side effects!

The Benefit of a healthy lifestyle
being an account of 30 years of research in Caerphilly
The challenge from Caerphilly to the people of Wales:

Take up one additional healthy behaviour.....
...cut smoking... reduce weight.... exercise more....
...check your diet.... reduce alcohol intake...

Then, when well embedded into your lifestyle, take up another healthy behaviour..... and reap the benefits now and into old age!

....and the undesirable effects?
....none for you
but an extra decade of care and cost for your children!
A medical research study in Caerphilly has shown a healthy lifestyle gives marked protection against diabetes, heart attacks, strokes, cancer and dementia.

In this website we offer advice and encouragement about how to develop a more healthy way of living and we encourage you to start by first taking just one additional healthy behaviour... and then another!

So do read on.......

On another website we give information about the health benefits to older people of a small daily dose of aspirin:
Dementia

In Caerphilly, the men who followed a healthy lifestyle had huge protection from loss of brain power - almost 70% less dementia!

And the men who followed a healthy lifestyle but still got dementia were, on average, seven years older that those who had followed none of the behaviours and got dementia.

A good principle is ‘Use it or lose it!’

If you really want to preserve your brain power then keep it active. Men who spend their leisure time actively lose much less nounce…. and face it…. sitting watching TV is not active leisure…. No way!

Source:

CONCLUSIONS

1. A healthy lifestyle is associated with large reductions in disease and disablement
   - only 5% of people in Wales follow a healthy lifestyle
   - yet a healthy lifestyle is under a subject's own control, costs nothing and has no undesirable side effects!
CONCLUSIONS

1. A healthy lifestyle is associated with large reductions in chronic disease
   - only 5% of people in Wales follow a healthy lifestyle
   - yet a healthy lifestyle is under a subject’s control, costs nothing and carries no undesirable side effects

2. Many factors are predictive of dementia
   - a healthy lifestyle is associated with a reduction of 50-60% in cognitive function and in dementia
   - hypertension, vascular disease and diabetes increase the risk, probably by 50 – 100%
     diabetes would seem to be of particular interest, increasing the risk by about 50%
     - almost 70% of new diabetes is attributable to overweight
   - good control of blood glucose reduces cognitive loss
   - intensive dietary intervention can achieve remission of diabetes (Lancet two weeks ago)
   - a high blood rheology appears to be a risk factor…. and this is testable
   - other factors – social support, hearing loss, sleep disturbance may be predictive

   but the independent association of these and other possible factors needs to be determined
CONCLUSIONS

1. A healthy lifestyle is associated with large reductions in chronic disease
   - only 5% of people in Wales follow a healthy lifestyle
   - but a healthy lifestyle is under a subject’s control, it costs nothing and carries no undesirable side effects

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3. There is no accepted definition of ‘wellbeing’
   - it is dependent upon the perception of health, of satisfaction, the level of self-efficacy, and a positive attitude
   - again, a healthy lifestyle appears to be associated with increases in some of these aspects

again, the independent association of these and other possible factors needs to be determined
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2. Many factors are predictive of dementia. A healthy lifestyle is associated with a reduction of 50-60% in cognitive function and in dementia. Hypertension, vascular disease and diabetes increase the risk, probably by 50-100%. Diabetes would seem to be of particular interest, increasing the risk by about 50%. Almost 70% of new diabetes is attributable to overweight. Good control of blood glucose reduces cognitive loss. Intensive dietary intervention can achieve remission of diabetes (Lancet tw weeks ago).

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3. There is no accepted definition of 'wellbeing'. It is dependent upon the perception of health, of satisfaction, the level of self-efficacy, and a positive attitude. Again, a healthy lifestyle appears to be associated with increases in some of these aspects. The independent association of these and other possible factors needs to be determined.

CONCLUSIONS
1. A healthy lifestyle is associated with large reductions in chronic disease - only 5% of people in Wales follow one - this proportion appears to have changed little over the past 35 years.

2. Many factors are predictive of dementia - a healthy lifestyle is associated with a reduction of 50–60% in cognitive function and in dementia - hypertension, vascular disease, and diabetes increase the risk, probably by 50–100%; diabetes would seem to be of particular interest, increasing the risk by about 50% - almost 70% of new diabetes is attributable to overweight - good control of blood glucose reduces cognitive loss - intensive dietary intervention can achieve remission of diabetes (Lancet tw weeks ago) - a high blood rheology appears to be a risk factor… and this is testable - other factors - social support, hearing loss, sleep disturbance may be predictive - the independent association of these and other possible factors needs to be determined.

3. There is no accepted definition of 'wellbeing' - it is dependent upon the perception of health, of satisfaction, the level of self-efficacy, and a positive attitude - again, a healthy lifestyle appears to be associated with increases in some of these aspects - again, the independent association of these and other possible factors needs to be determined.

CONCLUSIONS

HEALTHY LIVING? - WHAT A BLUNT INSTRUMENT!

- What about residual confounding?
- What about reverse causality?
- No biological mechanisms have been identified!
- No protein or enzyme can yet be been targeted!

Let's wait for better understanding.....

....let's wait for a silver bullet!
Healthy living

Better than any pill... no cost and no side effects!

and is additional, and not an alternative to any ‘silver bullet’!
‘……if only I had known the benefits of a healthy lifestyle.’