

Module 2:

Risk factors and reducing the risk



Contents

Risk factors known and implicated4

Information about risk and clinical practice7

Current controversies and issues9

Summary9

Resources10

References10

Module 2: Risk factors and reducing the risk

Introduction

Primary prevention of disease and illness is fundamental in our pursuit of wellness. To prevent dementia, an understanding of the cause and contributing factors is necessary. However, except for a very small group with a specific genetic makeup, there are not known factors that can be said to cause dementia. The evidence reveals that causation more likely depends on an accumulation of factors in any one person. Factors that contribute to the likelihood of an individual developing dementia have been identified; these fall into the categories of genetic and lifestyle risk. This module will explore risk factors for dementia and discuss strategies to address these, as well as focus on issues to take into consideration when introducing discussion about risk in health care practice.

Objectives

On successful completion of this module you will be able to:

- Outline the risk factors for developing dementia
- Describe strategies to minimise risk factors
- Debate issues about introducing discussion of risks for dementia to clinical practice

Module topics

Risk factors – known and implicated
 Reducing the impact of identified risks
 Considerations in offering information about risk
 Current controversies and issues
 Current research
 Summary
 References

Suggested reading for this module

Alzheimer's Australia. (2012). *Genetics of Dementia*. Dementia Q&A Help Sheet 12. Alzheimer's Australia: Canberra.
http://www.fightdementia.org.au/common/files/NAT/20121211_NAT_UpdateSheet_DementiaQA12_Genetics.pdf

Loy, C. T., Schofield, P. R., Turner, A. M., & Kwok, J. B. J. (2014). Genetics of dementia. *Lancet*, 383(9919), 828–840.

Tanzi, R. E. (2013). A brief history of Alzheimer's disease gene discovery. *Journal of Alzheimer's Disease* 33: S5–S13.

Farrow, M., & O'Connor, E. (2012). *Targeting brain, body and heart for cognitive health and dementia prevention*. Alzheimer's Australia: Canberra.
http://www.fightdementia.org.au/common/files/VIC/YBM_evidence_paper_29_lores.pdf

Simons, L. A., Simons, J., McCallum, J., & Friedlander, Y. (2006). Lifestyle factors and risk of dementia: Dubbo Study of the elderly. *Medical Journal of Australia*, 184(2), 68–70.

http://www.mja.com.au/public/issues/184_02_160106/sim10682_fm.html

Lautenschlager, N. T., Cox, K., & Cyarto, E. V. (2012). The influence of exercise on brain ageing and dementia. *Biochimica et Biophysica Acta*, 1822: 474–481. Accessed online 19 June 2014 at <http://www.sciencedirect.com/science/article/pii/S0925443911001633>

Tyas, S. L., Salazar, J. C., Snowdon, D. A., Desrosiers, M. F., Riley, K. P., Mendiondo, M. S., & Kryscio, R. J. (2007). Transitions to mild cognitive impairments, dementia and death: Findings from the Nun study. *American Journal of Epidemiology*, 165(11), 1231–1238.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2516202/>

Risk factors known and implicated

Age

Age provides the greatest risk for developing dementia. In Module 1 the Australian demographic—reflecting most other countries that enjoy life longevity—clearly shows that as we age our risk of developing dementia increases. However, there are still many people who do not develop dementia despite living to record-breaking ages. This indicates probable potential to delay, or maybe even eradicate, the onset of dementia if the risks are identified and eliminated.

Genetic

Most of the research about dementia and risk has focused on Alzheimer's disease and there is still much to learn about the genetic basis of dementia.

Genes identified in the aetiology of Alzheimer's disease fall into two groups: autosomal dominant genes and susceptibility genes. Loy et al. (2013) provide a good overview of the genetics of dementia, particularly familial dementias caused by autosomal dominant genetic mutations. Tanzi (2013) provides an overview of the history of discovery of susceptibility genes for Alzheimer's disease.

Mutations in the autosomal dominant genes, amyloid precursor protein gene (APP), Presenilin 1 and Presenilin 2 (PS1 & PS2) are known to cause Alzheimer's disease. These are rare and account for 1% of cases and development is typically younger onset (<65 years) disease.

More than three dozen susceptibility genes have been identified; the major one being the $\epsilon 4$ variant of the Apolipoprotein E (APOE) gene. Having the susceptibility gene(s) predisposes a person to developing Alzheimer's disease; however, a variety of factors appear to attenuate this predisposition such as protective lifestyle behaviours. The identified genes are thought to play roles in the metabolism of amyloid (the protein that forms plaques in Alzheimer's disease), lipid metabolism, immunity and cell communications. Having one copy of APOE $\epsilon 4$ increases risk for dementia four times, while having two

copies increases risk ten times. Other susceptibility genes have a much smaller impact on risk.

People with a genetic predisposition to vascular disease will also show a predisposition to vascular dementia. Therefore, any behaviour that protects the integrity of the vascular system, thus preventing infarcts, will be beneficial to reducing the incidence of this type of dementia. As many dementias are of a mixed variety, and vascular disease can exacerbate dementia whose primary cause is Alzheimer's disease or another brain disease, reducing vascular risk factors will also reduce the incidence of other dementias. Many behaviours that are suggested to reduce the incidence or delay the onset of dementia are behaviours that would also be promoted in any healthy approach to life.

Activity

Consider how would you respond to a client/family member who came to you to ask about their risk of developing dementia when they have a maternal and paternal grandparent with dementia?

Alzheimer's Australia provides a help sheet summarising the evidence on the genetics of dementia. This can be a useful tool to use in guiding your discussions with families who would like to know more about familial dementia or genetic risk.

http://www.fightdementia.org.au/common/files/NAT/20130912_NAT_HS_AboutDementiaHelpSheet_10.pdf

Lifestyle

Lifestyle factors are difficult to study in our search for the cause(s) of dementia. Lifestyle practices result in many interactions, and outcomes may result from these interactions rather than any individual factors (i.e., the whole is greater than the sum of the parts). An Australian longitudinal lifestyle study was conducted in Dubbo, NSW, which aimed to identify factors that may predict an increase in dementia risk.

Read *Lifestyle factors and risk for dementia: Dubbo study of the elderly* by Leon Simons et al. (Listed in suggested readings for this module.)

Activity

Although conducted some time ago, this study is of interest because it was conducted in Australia and findings are consistent with other world-wide studies on dementia risk. In addition, study results contribute weight to recommendations that aim to reduce the national incidence of dementia. Findings can be divided into protective and increased risk factors.

Protective factors against dementia identified in the Dubbo study include:

- Higher education
- Daily exercise: for example, walking, gardening
- Moderate alcohol intake:¹

For healthy men and women no more than two standard drinks on any day reduces the risk of harm from alcohol-related disease or injury over a lifetime. Drinking no more than four standard drinks on a single occasion reduces the risk of alcohol-related injury arising from that occasion.

The alcohol guidelines are based on healthy adults. Factors such as gender, age, mental health, drug use, and existing medical conditions can change how alcohol affects a person. National guidelines for alcohol have been developed by the National Health and Medical Research Council (NHMRC, 2009)

<http://www.nhmrc.gov.au/files/nhmrc/file/publications/synopses/ds10-alcohol.pdf>

Factors associated with increased risk in the Dubbo study include:

- Prior coronary heart disease
- Impaired peak expiratory flow (PEF)
- Poor self-rated health
- Physical disability
- Depression
- Moderate to severe head injury.

Systematic reviews and meta-analyses have identified additional risk and protective factors. Smoking, diabetes, hypertension, midlife high cholesterol, midlife obesity and being underweight are associated with increased dementia risk. Cognitively stimulating lifestyles and the Mediterranean diet are associated with reduced dementia risk. For a summary of research in this area, see the Alzheimer's Australia paper by Farrow and O'Connor (listed in suggested reading for this module).

Professor Nicola Lautenschlager has published widely on the topic of exercise and risk reduction. A summary of her study which found exercise improved memory in older people with memory complaints can be found in a news report at

<http://www.abc.net.au/science/articles/2008/09/03/2353939.htm>.

Professor Lautenschlager's latest study (2013) published in *Neurodegenerative Disease Management* found emerging evidence that physical activity is good for both mild cognitive impairment and

¹ Light to moderate alcohol consumption in older adults may lower the risk of several chronic conditions. However, for some older adults, drinking alcohol increases the risk of falls and injuries, as well as some chronic conditions. Older people are advised to consult their health professionals about the most appropriate level of drinking for their health. (NHMRC)

dementia but concluded that more randomised controlled trials are needed.

Clearly, a lifestyle that is generally healthy, promoting cardiovascular, respiratory and cerebrovascular health may reduce risk for dementia. In addition, it would seem a relaxed lifestyle with moderate alcohol intake may contribute to a dementia reducing strategy. The promotion of the 'clever country', often a strategy to make Australia internationally competitive, may also have a place in this strategy.

Alzheimer's Australia's *Your Brain Matters* is a useful resource to guide patients/clients who would like further information on preventing dementia. This might be particularly relevant for those who have a family history of dementia. Based on the evidence discussed above, it recommends mental stimulation, physical activity, healthy diet, and effective control of cardiovascular risk factors for reducing dementia risk. <http://yourbrainmatters.org.au/>

As discussed in Module 1, mild cognitive impairment (MCI) can occur without progressing to dementia. Some people have lived with MCI for years without evidence of progression. This observation is of interest as it may provide an opportunity to uncover treatments that could delay the progression of dementia and maintenance of independence. Research findings indicate older age, poorer cognition, lower education and the presence of the APOE $\epsilon 4$ allele may be associated with progression from MCI to dementia within a few years.

An interesting, longitudinal study conducted in the United States on a cohort of nuns aimed to find out more about the relationship between MCI and dementia (Tyas et al., 2007). Transitions to mild cognitive impairments, dementia and death: Findings from the Nun study.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2516202/>

Information about risk and clinical practice

Read *Transitions to mild cognitive impairments, dementia and death: Findings from the Nun Study* by Suzanne Tyas et al. (2007).

In this study, older age, low education and the presence of the APOE $\epsilon 4$ allele were all shown to increase the risk of MCI and of dementia, but only age increased risk of progression from MCI to dementia during the seven years of follow-up. The authors of this study concluded that MCI is consistent with early dementia and that risk factors for dementia appear to start people on the road to dementia, with subsequent progression to dementia depending on age. Further findings from this and similar studies will be interesting in advancing our knowledge about dementia, and how we deal with clients who present with MCI. For example, the Australian Imaging, Biomarker and Lifestyle (AIBL) Flagship Study of Ageing is a longitudinal study of over 1000 older Australians, assessed every 18 months, contributing

Activity

to our understanding of the development and progression of Alzheimer's disease through preclinical and clinical stages.

<https://aibl.csiro.au/>

No-one welcomes the possibility that they will experience dementia. In fact, dementia is well-placed within the top 10 health conditions that people fear they may develop (coming second to cancer). We are bombarded on a daily basis with information on how we can reduce our risk of disease; how we relate to this depends more on our personal situation and history than it does on the population statistics presented.

Consider the following 10 conditions:

Cancer, heart disease, stroke, neurodegenerative disease, blindness, dementia, amputation, quadriplegia, endogenous depression, and autoimmune disease.

Activity

Without thinking too much about it, order these from 1 to 10 based on the most feared to the least feared.

Now reflect on and explain why you have ordered the conditions in the way you have.

Generally, assessment of risk will be based to some degree on the fears you hold. However, these fears are based on many other things; for example, stigma, previous experience of the condition in family members or friends, context of the risk and belief systems held, such as whether good health is within personal control or not. The experience of symptoms that may be related to the risk will also contribute to the immediacy and emotional tenor of the assessment. Experience, age and emotion often modify the meaning of a risk and most people will react to risk threat based on this meaning (Walter & Britten, 2002). For the clinician, interpreting risk comes with risks in itself. What does the client need to know? What does the client want to know? How is the client going to understand or use risk information offered? Is the information offered going to add more burden to the 'worried well' in our community? What is the best way to offer information about risk?

Kenneth Calman's (2001) paper Issues of risk: 'this unique opportunity' is very broad in its application; however, many considerations about the impact of risk are offered. In discussing risk in clinical practice, Calman cautions that a dialogue must occur. Information is ideally offered in an informed way for each person. We need to consider:

- What is the client asking for information about?
- What is the level of emotion evident in the request for information?
- What is the scientific evidence? And how can this evidence be offered in a way that will be understood by this person?

- How can strategies that are possible/feasible for the person's lifestyle be implemented? How do they discuss their investment in the future – in financial or self-management terms or their ability to create a legacy?
- Are we avoiding this client's questions or requests because we are fearful of emotional outburst?
- What suggestions can be offered that enables this person to deal with the evidence?

There is still much to be learnt about risks relating to dementia. Even if one were to test positive for the APOE ϵ 4 allele, what then? Can we do more than advise the client to live according to current good general health guidelines (see the Alzheimer's Australia *Your Brain Matters* website, <http://yourbrainmatters.org.au/>) and to keep their affairs in order—something that is currently being promoted in healthcare circles generally (see Module 5: *Social and lifestyle considerations* and the *Respecting Patient Choices* website at <http://www.respectingpatientchoices.org.au/> for more information).

People who have concerns about the development of dementia need to be encouraged to voice their concerns and have these addressed in light of the evidence and what can be done, and the uncertainty that exists in relation to these concerns.

Current controversies and issues

- Relative importance of the described risk factors in the causation of dementia and whether management of risk factors prevents disease onset and/or disease progression
- Translation of epidemiological studies to the clinical setting for individual patients
- Family, client and clinician' desire for a treatment creates an environment where critical appraisal of research evidence may be compromised
- Role and appropriateness of complementary therapies, especially given the perception that these therapies are harmless
- Screening for risk factors including APOE ϵ 4 status and other genetic markers in terms of benefit to the individual patient are contentious and problematic

Summary

This module has identified a number of recognised and postulated factors that place an individual at risk of developing dementia and has presented a discussion as to how these risk factors might be addressed. This area of investigation continues to develop and the knowledge base will need to improve substantially before firm recommendations for individuals are possible in the clinical setting.

The use of low-cost interventions that have other social and health benefits can be supported; these include physical exercise, a healthy

diet, mental stimulation and social inclusion. Effective control of cardiovascular risk factors and management of depression are also likely to be important.

More contentious interventions such as nutritional supplements require a balanced approach involving a discussion between client and clinician. The use of such therapies is not currently supported by clinical trial evidence and is therefore a personal lifestyle decision. The role of the clinician is to ensure clients have the information available and make an informed decision.

Resources

Alzheimer's Australia: *Your Brain Matters* program

<http://yourbrainmatters.org.au/>

Alzheimer's Australia: *Dementia Q&A Help Sheet 7 What You Eat and Drink and your Brain*

http://www.fightdementia.org.au/common/files/NAT/20121211_NAT_UpdateSheet_DementiaQA7_EatAndDrink.pdf, June 2011

Alzheimer's Australia: *Dementia Q&A Help Sheet 6 Mental Exercise and Dementia*

http://www.fightdementia.org.au/common/files/NAT/20121211_NAT_UpdateSheet_DementiaQA6_MentalExercise.pdf

Alzheimer's Australia: *Dementia Q&A Help Sheet 8 Physical Exercise and Dementia*

http://www.fightdementia.org.au/common/files/NAT/20121211_NAT_UpdateSheet_DementiaQA8_PhysicalExercise.pdf,

Dementia Collaborative Research Centres: *Early Diagnosis and Prevention Centre* <http://www.dementiaresearch.org.au/the-centres/8-about-us/226-dcrc-edp.html>

Lautenschlager, N. T., Almeida, O. P., & Flicker, L. (2003). Preventing dementia: why we should focus on health promotion now. *International Psychogeriatrics*, 15(2), 111-119.

Pathways to the Future 2006 and Beyond. Dementia framework for Victoria Department of Human Services, p. 21

http://www.health.vic.gov.au/agedcare/downloads/dementia_policyframework.pdf

References

Calman, K. (2001). Issues of risk: 'this unique opportunity'. *British Journal of*

General Practice, 51, 47-51.

Lautenschlager, N. T. (2013) Physical activity and cognition in older adults with mild cognitive impairment and dementia, *Neurodegenerative Disease Management*, Vol. 3, No. 3, Pages 211-218. Doi: 10.2217/nmt.13.26. Accessed online 19 June 2014 at

<http://www.futuremedicine.com/doi/abs/10.2217/nmt.13.26>

Walter, F. M., & Britten, N. (2002). Patients' understanding of risk: a qualitative study of decision-making about the menopause and hormone replacement therapy in general practice. *Family Practice*, 19(6), 579–586.