



The Brain–Body Connection: GCBH Recommendations on Physical Activity and Brain Health

Global Council on
Brain HealthSM
A COLLABORATIVE FROM **AARP**

Introduction

The Global Council on Brain Health (GCBH) is an independent collaborative of scientists, health professionals, scholars and policy experts from around the world working in areas of brain health related to human cognition. The GCBH focuses on brain health relating to peoples' ability to think and reason as they age, including aspects of memory, perception and judgment. The GCBH is convened by AARP with support from Age UK to offer the best possible advice about what older adults can do to maintain and improve their brain health. GCBH members come together to discuss specific lifestyle issue areas that may impact peoples' brain health as they age with the goal of providing evidence-based recommendations for people to consider incorporating into their lives.

We know that many people across the globe are interested in learning what they can do to maintain their brain health as they age. We aim to be a trustworthy source of information basing recommendations on current evidence and supplemented by a consensus of experts from a broad array of disciplines and perspectives. We intend to create a set of resources offering practical advice to the public, health care providers, and policy makers seeking to make and promote informed choices relating to brain health.

Physical Activity and Brain Health

On April 14, 2016 members of the GCBH met to critically examine the impact of physical activity on brain health. A list of participants and GCBH members are included in Appendix 1. The purpose was to interpret current scientific evidence and generate actionable recommendations. This paper provides a summary of the consensus reached by the experts and describes the process they went through to reach the recommendations. This paper was not intended to be a systematic, exhaustive review of all pertinent scientific literature on the topic of physical activity and brain health. Rather, the selected references provided at the end give helpful background material and present a sizable sample of the current evidence base underpinning the GCBH's consensus in this area.

The experts at the meeting reached consensus on five statements summarizing their opinions about the current state of the evidence base on the relationship of physical activity to brain health as people age. The participants then provided recommendations as well as practical tips for individuals based upon their expert opinions. These statements and recommendations along with the summary of the discussion were circulated amongst other members of the GCBH, and reviewed by other experts in the field. As a result of these deliberations, on July 15, 2016 the GCBH Governance Committee approved the following recommendations on physical activity and brain health for people as they age.

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Before engaging in a new exercise routine, the GCBH recommends consulting with your doctor.

Executive Summary of the Consensus and Recommendations

Expert Consensus

1. Physical activity has a positive impact on brain health.
 - a. A physically active lifestyle (e.g. walking, using the stairs, gardening, etc.) provides benefits for brain health.
 - b. Purposeful exercise (e.g. brisk walking, cycling, strength training, group exercise classes, etc.) provides benefits for brain health.
3. People can change their behavior to become more physically active at any age.
4. Based on randomized controlled trials, people who participate in purposeful exercise show beneficial changes in brain structure and function.
5. Based on epidemiological evidence, people who lead a physically active lifestyle have lower risk of cognitive decline.¹
6. In spite of the link between physical activity and brain health, there is not yet sufficient scientific evidence that physical activity can reduce risk of brain diseases that cause dementia (e.g. Alzheimer's disease).

¹ What the GCBH means by "risk" and "risk reduction" is defined in the attached Glossary in Appendix 2.

² The GCBH considered and discussed the public health guidelines on physical exercise issued by governmental agencies or professional societies from participants' countries of origin (Australia, Canada, Singapore, the United Kingdom, and the United States.). Each entity made similar recommendations, but for purposes of this summary, the United States' Centers for Disease Control and Prevention (CDC) guidelines have been selected as the primary reference. References to all guidelines considered are provided in Appendix 3.

Expert Recommendations

1. For purposeful exercise, follow current public health recommendations of 150 minutes of weekly, moderate-intensity aerobic activity and two or more days a week of moderate-intensity, muscle-strengthening activities.² In addition to purposeful exercise, lead a physically active lifestyle throughout the day.
 - a. Identify what exercises or activities you may already do and do more unless you are already extremely active.
 - b. Try new physical exercises and physical activities that you think that you will enjoy.
 - c. Engage in strength training and exercises that improve flexibility and balance in addition to aerobic exercise; a variety of physical activities is better than one kind alone.
 - d. In a safe community or area, walk to your destination, or park farther away from the entrance of wherever you are going.
 - e. Take the stairs instead of the elevator.
 - f. Communities should consider closing streets on holidays and weekends to encourage biking, walking, and other physical activities in public spaces on a regular basis.
 - g. Get moving throughout your day.
2. Identify meaningful and enjoyable ways to increase and maintain physical activity.
 - a. Know that whatever your age or current health status, there are options to be physically active.
 - b. Challenge yourself a little bit more over time, for example:
 - III. If you are not very active, start stretching and walking at a leisurely pace.
 - IV. If you are already a walker or jogger, increase your pace or distance.
 - V. If you are an active runner, keep running and start strength/resistance training.
 - c. Be patient and persistent.
 - d. To stay motivated, consider doing physical activities with other people. Social aspects of physical activity can help inspire you to continue your efforts.
 - e. Make concrete plans to move your body – think about when, where and with whom you will be physically active.
3. Incorporate physical activity as a part of a healthy lifestyle to help reduce the risk of cognitive decline.
4. When focusing on the impact of physical activity on brain health, stakeholders and policy makers should take into account the breadth of scientific evidence (i.e. animal studies, epidemiological studies, and randomized controlled trials) while recognizing the knowledge gaps.

Process

Issue specialists were selected to participate with the GCBH because they are considered leaders in their fields who have conducted research that has significantly contributed to the body of evidence connecting physical activity with brain health. The diverse areas of their expertise represent different perspectives and disciplines including gerontology, internal medicine, psychology, physical therapy, epidemiology, sports psychology, exercise physiology, neuroscience, psychogeriatrics, and public health.

Eight issue specialists from four continents were asked to critically examine the state of the science as of April 2016. They discussed findings from both animal and human research (ranging from observational and epidemiological studies to randomized controlled trials) and considered the cumulative body of evidence to determine whether it is sufficient to issue physical activity recommendations for individuals to maintain and improve brain health. The issue specialists considered the following questions as a framework to guide their deliberations:

1. Does exercise help your brain function better as you age? How? What type is best?
2. What do we know about how often and how long?
3. Can we see change in the brain after exercise?
4. Can exercise stop cognitive decline and disease?
5. Can we motivate behavior change to promote sustained exercise for all people?
6. What level of evidence do we need to make recommendations on exercise and brain function?

(The complete set of more detailed questions is available in Appendix 4)

After an in-depth moderated discussion, the issue specialists arrived at five statements to summarize the impact of physical activity on brain health. Based on their consensus, they made four recommendations related to physical activity in the context of brain health and cognitive decline. They further agreed on practical tips to integrate physical activity and exercise into peoples' daily lives to promote their brain health.

Liaisons from civic and non-profit organizations with relevant expertise in brain health and physical exercise were invited to provide input and technical feedback during the Governance Committee's refinement of the draft recommendations.

Five Governance Committee members participated during the in-person meeting. The entire Governance Committee reviewed and finalized the document during subsequent conference calls in May 2016. The Governance Committee issuing the recommendations are also independent health professionals representing diverse expertise in epidemiology, public health, neurology, psychiatry, geriatrics, cognitive neuroscience, neuropsychology, pharmacology, medical ethics and health policy, and neurodegeneration.

The Governance Committee applied their expertise to determine whether they concurred with the statements and to evaluate the objectivity and feasibility of the proposed recommendations. The GCBH Governance Committee reviewed this summary document to decide whether it accurately reflected the expert opinions expressed and the current state of science in the field. The Governance Committee approved the document on July 15, 2016.

Discussion

I. Guiding principles underlying the expert consensus and recommendations

Science and knowledge of brain health are continually evolving. These recommendations are based upon the current state of scientific and medical knowledge as of April 2016 in order to provide people with reliable information on what is known and not yet known about the relationship between physical activity and brain health.

These recommendations are meant for all adults, particularly focusing on those 50 and older who have not been diagnosed with a neurodegenerative disease such as Alzheimer's. The intent is to be as inclusive as possible for all people as they age. The GCBH panel did not focus on the body of research related to the impact of physical activity on people diagnosed with neurodegenerative diseases. However, in general, regardless of diagnosis, if an individual is physically capable, the GCBH recommends physical activity to benefit their brain health.

II. Contextual factors matter in tailoring recommendations to any particular individual

Individual Assessment

Recommendations for physical activity to maintain or improve brain health need to be tailored to the individual to take into account his or her current state of health, fitness, and readiness to exercise. Individuals' physical environment and what is practically and economically feasible must also be factored into their plans to sustain regular physical activity. For safety reasons, it is always advisable to consult with a health care provider before beginning or significantly changing an exercise regimen.

of regularly engaging in physical activity. Urban design and livable communities, therefore, can strongly influence the ability and willingness of older adults to engage in physical activity.

Communities

The physical environment — for example, how walkable a community is (i.e. the presence of sidewalks, safe environment) — plays an important role in the feasibility

Cultural norms, beliefs, and values within communities can similarly impact an individuals' desire to take part in purposeful exercise and to choose an active lifestyle. Given that regular physical activity can be challenging for many people to sustain, finding and promoting activities supported and facilitated within communities where individuals live is important to help them maintain such activity. For example, accessible, free and climate controlled shopping malls with walking programs have been shown to promote physical activity for older adults.

III. Comparing different types of physical activity that have positive impacts on brain health

The discussion amongst the experts emphasized that physical activity comprises both purposeful exercise and active lifestyle. Therefore the GCBH recommended that people do both to maintain and improve brain health. Those who provided advice within their own clinical practices said that many of their clients wondered what types of physical activity would be good for the brain. The following chart compares and contrasts the different types of physical activities and provides some common examples of what is meant by each.

Purposeful Exercise Moderate to Vigorous Exertion	Active Lifestyle An attitude to incorporate movement in day-to-day activities
<i>Examples include:</i>	<i>Examples include:</i>
<ul style="list-style-type: none">• Walking at a brisk pace to increase your heart rate• Strength/resistance training (e.g. free weights, squats, lunges)• Aerobic training which raises your heartrate (e.g. cycling, jogging, running, swimming laps, group exercise classes)	<ul style="list-style-type: none">• Walking to work or the store instead of driving• Taking the stairs instead of the elevator• Parking farther away from your destinations• Engaging in hobbies and sports such as active yoga, dancing, gardening

IV. There is not consensus on what types of exercises are optimal for brain health

Current international public health guidelines recommending 150 minutes of weekly, moderate intensity purposeful aerobic exercise including strength training are based on cardiovascular research. See Appendix 3. To date, public health authorities have not issued physical exercise guidelines specifically for promoting brain health. Research and recommendations regarding the duration and intensity of exercise that may lead to optimal brain health would therefore significantly advance understanding in this area of health. It is clear, however, that recommendations on duration and intensity of exercise should always be adapted to an individual level based on personal factors, including level of frailty and current fitness.

Despite not being able to conclude which types of exercise are better than others based on current evidence, research indicates that people who are less active can benefit their brain health by becoming more active. For example, evidence indicates that individuals who lead inactive or sedentary lifestyles stand to benefit more from an increase in physical activity than those who are already physically active and take up a new exercise regimen. Even without consensus on the optimal type of exercise, all the participants recommend that people should start thinking about the type, frequency, duration and intensity of exercise they currently get either at work or in leisure time, and consider how they could increase or vary that. If an individual is sedentary during the day, standing up and taking walking breaks is helpful.

V. Nature of evidence considered

During the April 14 convening, the experts examined and weighed data from a range of studies including animal research, epidemiological studies, and randomized controlled trials. Animal research allows scientists to test the mechanisms that underlie an exercise intervention, allowing them to quickly determine whether an intervention can result in meaningful biological changes. Human epidemiological studies can provide clues to characteristics or behaviors that can improve or worsen health. Although epidemiological studies do not establish causality between exercise and cognitive health, they evaluate exercise in more realistic settings and over longer periods of time than are practical with randomized controlled trials. Randomized controlled trials (RCTs) test if an intervention results in changes in health in those randomly assigned to the intervention (such as exercise) compared to those who did not get the intervention. Both epidemiological and RCT studies are used to generate evidence for scientists to establish links between behavior and outcomes, but each of these types of

studies has its strengths and limitations. A comparison of the strengths and weaknesses of the two different study types in humans is provided in Appendix 5.

Relevant to the current consensus statement, findings from multiple epidemiological studies over the past 20 years show that an individual with a lifelong history of being physically active has a lower-than-average risk of cognitive decline with aging. In addition, RCTs have shown that purposeful exercise can bring about positive changes in the brain in relatively short amounts of time (6-12 months). However, RCTs of physical activity have not, to date, been successful in showing a reduction in the risk of dementia. Thus, epidemiological studies and RCTs which examine brain changes suggest that increased physical activity has a positive impact on the brain, but available data from RCTs are currently limited in making conclusions about whether physical activity may reduce the risk of dementia.

VI. Knowledge gaps

There are many areas where we need more evidence related to physical activity and brain health before GCBH members can provide more detailed recommendations. Additional research, which includes diverse samples, would be very helpful to learn more about the optimal type, duration, and frequency of physical activity. Examples of helpful research for the future are listed below.

Future research is needed to fill knowledge gaps related to understanding the impact of different types of exercises (aerobic, resistance, stretching, and coordinative exercise) on brain health.

More evidence is needed to assess the benefits of coordinative exercises that involve cognitive processes and three dimensional movements, such as tai chi and dance. There is some evidence that has shown these kinds of exercises positively impact the brain.

Strength training and aerobic exercise may provide complementary benefits for physical health, but most of the studies providing evidence for the effects of purposeful exercise on brain health have been limited to aerobic exercise.

Although much has been learned from animal studies demonstrating the biological mechanisms by which exercise influences brain health, and neuroimaging has shown impact of physical exercise on the structure of the human brain, knowledge gaps remain regarding the underlying mechanisms by which exercise impacts the brain in humans.

Prolonged sitting is believed to be bad for the body, but there are no known studies demonstrating the harm or benefits of sitting on brain health.

There is not enough evidence to conclude how stretching exercises affect the brain. In most published randomized controlled trials relating to physical exercise, the control group (that is, the group who did not receive the tested-for intervention) consists of people who are engaged in stretching and toning activities.

Resistance training is known to be good for the cardiovascular system – and it helps in insulin regulation. However, the biological mechanisms by which resistance training impacts the brain in humans are still unknown.

There is not yet evidence indicating what types of exercise are good, better, or best. There are too few comparative dose response studies describing the effects of the quantity and quality of exercise on the brain. Therefore, we cannot say what the best combination of factors of physical activity such as duration, frequency, or intensity of exercise is necessary to achieve optimal brain health.

There is insufficient evidence at this time to conclude that exercise prevents the development of dementia such as that caused by Alzheimer’s disease. However, sufficient evidence has emerged to establish that physical activity promotes brain health.

Conclusion

As the population ages, more and more people are interested in what they can do to maintain their brain health. An abundance of sources is now available for people to find information, but it can be difficult to ascertain what the weight of current science says when new and sometimes conflicting studies are reported. The GCBH makes its recommendations to help people know what practical steps they can take to foster better brain health and feel confident they are taking them based upon reliable and scientifically sound information. Knowing there is a link between physical activity and staying mentally fit may help motivate people to increase physical activity as they age.

The consensus statements and recommendations above are based on the current state of science as of April 2016. As further developments occur in the study of the impact of physical activity on brain health, the GCBH will periodically revisit these recommendations and provide updates when appropriate.

List of Appendices

1. Participants, with suggested List of Additional Resources
2. Glossary
3. Citations to Public Health Authorities' Recommendations Regarding Physical Health
4. Discussion Questions
5. Differences, Strengths and Limitations of Two Study Types in Humans
6. Disclosure Statement of Potential Conflicts of Interest
7. Funding
8. Selected References

1. Participants

Members of the Global Council on Brain Health are independent health care professionals and experts coming from a variety of disciplines. The physical exercise issue specialists and Governance Committee members formulated these recommendations, the Governance Committee approved them.

Issue Specialists

Kirk Erickson, Ph.D.
University of Pittsburgh, USA

Arthur F. Kramer, Ph.D.
University of Illinois, USA

Nicola Lautenschlager, M.D.
University of Melbourne, Australia

Teresa Liu-Ambrose, Ph.D, P.T.
University of British Columbia, Canada

Ng Tze Pin, M.D.
National University of Singapore, Singapore

Marcus Richards, Ph.D.
University College London and Medical Research Council, UK

Kaycee Sink, M.D., MAS
Wake Forest School of Medicine, USA

Claudia Voelcker-Rehage, Ph.D.
Technische Universitaet Chemnitz, Germany

Governance Committee

Marilyn Albert, Ph.D.
Johns Hopkins University, USA (Chair)

Linda Clare, Ph.D., Sc.D.
University of Exeter, UK (Vice Chair)

Kaarin Anstey, Ph.D.
Australian National University, Australia

Martha Clare Morris, Sc.D.
Rush University, USA

Peggye Dilworth-Anderson, Ph.D.
University of North Carolina – Chapel Hill, USA

S. Duke Han, Ph.D., ABPP-CN
University of Southern California, USA

Yves Joannette, Ph.D.
University of Montreal, Canada

Jason Karlawish, M.D.
University of Pennsylvania, USA

Miia Kivipelto, M.D., Ph.D.
Karolinska Institutet, Sweden

Jessica Langbaum, Ph.D.
Banner Alzheimer's Institute, USA

Jacobo Mintzer, M.D.
Medical University of South Carolina, USA

Ronald Petersen, M.D., Ph.D.
Mayo Clinic, USA

Kate Zhong, M.D.
Cleveland Clinic Lou Ruvo Center for Brain Health, USA

Moderator

James Hamblin, M.D.
The Atlantic

Staff

Betsy Agnvall
AARP

Nicholas Barracca
AARP

Lindsay R. Chura, Ph.D.
AARP

James Goodwin, Ph.D.
Age UK

William Hu, M.D., Ph.D.
Emory University, and Consultant to GCBH

Sarah Lenz Lock, J.D.
AARP

Logan Ruppel
AARP

Debra B. Whitman, Ph.D.
AARP

Other experts from relevant public agencies and non-profit associations provided guidance and feedback to help shape of these recommendations. Grateful acknowledgment goes to:

Liaisons

Debra Babcock, Ph.D. M.D.
*National Institute for Neurological Disorders and Stroke**

Matthew Baumgart
Alzheimer's Association (USA)

Basia Belza, MSN, Ph.D.
University of Washington

Colin Capper
Alzheimer Society (UK)

Ann-Hilary Heston
YMCA

Jeremy Hughes
Alzheimer Society (UK)

Sarah Ingersoll, MBA
University of Southern California

Cara Johnson, YMCA

Melinda Kelley, Ph.D.
*National Institute on Aging**

Valerie A. Lawson, MS, RD, LDN
YMCA

Lisa McGuire, Ph.D.
*Centers for Disease Control and Prevention**

Jane Tilly, Dr.PH
*Administration for Community Living**

Molly Wagster, Ph.D.
*National Institute on Aging**

Joan Weiss, Ph.D., RN, CRNP
*Health Resources and Services Administration**

Sara Wilcox, Ph.D.
University of South Carolina

Participants and Liaisons' List of Additional Resources

Go4Life, <https://go4life.nia.nih.gov/>

The Brain Health Resource, http://www.acl.gov/Get_Help/BrainHealth/Index.aspx

<https://www.nia.nih.gov/alzheimers> (main web page for the National Institute on Aging)

https://d2cauhfh6h4xop.cloudfront.net/s3fs-public/preventing_alzheimers_disease_o.pdf ("Preventing Alzheimer's Disease: What Do We Know?")

American College of Sports Medicine, Position Stand on Exercise and Physical Activity for Older Adults, http://journals.lww.com/acsm-msse/Fulltext/2009/07000/Exercise_and_Physical_Activity_for_Older_Adults.20.aspx

Alzheimer's Society factsheet on Exercise and Physical Activity, https://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=1764

National Council on Aging, <https://www.ncoa.org/center-for-healthy-aging/physical-activity/physical-activity-programs-for-older-adults/>

Surgeon General's Call to Action, Step It Up! <http://www.surgeongeneral.gov/library/calls/walking-and-walkable-communities/exec-summary.html>

*Participation in this activity by these individuals does not necessarily represent the official viewpoint of the U.S. Department of Health and Human Services, the National Institutes of Health, or the National Institute on Aging.

2. Glossary

The purpose of the glossary is to highlight how the GCBH used these terms within the context of their discussions and in this document.

Absolute intensity. The amount of energy used by the body per minute of activity.

Aerobic. Activity in which the body's large muscles move in a rhythmic manner for a sustained period of time. Aerobic activity, also called endurance activity, improves cardiorespiratory fitness. Examples include walking, running, and swimming, and bicycling.

Brain Health. The mental process of cognition including the abilities to think, reason, learn, remember, concentrate, use judgment and plan.

Cognitive Decline. The Institutes of Medicine (IOM) in 2015 defined a similar term, cognitive aging, as the lifelong process of gradual and ongoing, yet highly variable change in cognitive functions that occur as people get older. Cognitive decline is a term used by the experts to describe the trajectory of losing cognitive abilities absent of a specific disease or condition.

Confounder. A situation in which the effect or association between an exposure and outcome is distorted by the presence of another variable.

Coordinative exercise/Balance training. Static and dynamic exercises that are designed to improve individuals' ability to withstand challenges from postural sway or destabilizing stimuli caused by self-motion, the environment, or other objects.

Dementia. Dementia isn't a specific disease. Instead, dementia describes a group of symptoms affecting memory, thinking and social abilities severely enough to interfere with daily functioning. Though dementia generally involves memory loss, memory loss has different causes. So memory loss alone doesn't mean you have dementia.

Alzheimer's disease is the most common cause of a progressive dementia in older adults, but there are a number of causes of dementia. Depending on the cause, some dementia symptoms can be reversed.

Epidemiological studies (which can be cross-sectional or longitudinal). These studies are observational in nature where scientists try to establish a link between lifestyle activities over time (e.g., regular exercise) and long-term outcomes (brain health with aging).

Frailty. This term is defined as a clinically recognizable state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with every day or acute stressors is compromised.

Intensity. Intensity refers to how much work is being performed or the magnitude of the effort required to perform an activity or exercise. A frequently used way of distinguishing between moderate and vigorous activity is that if you can talk while performing it, it's moderate. If you need to stop to catch your breath after saying just a few words, it's vigorous. More formal definitions are:

Baseline activity. The light-intensity activities of daily life, such as standing, walking slowly, and lifting lightweight objects. People who do only baseline activity are considered to be inactive.

Health-enhancing physical activity. Activity that, when added to baseline activity, produces health benefits. Brisk walking, jumping rope, dancing, playing tennis or soccer, lifting weights, climbing on playground equipment at recess, and doing yoga are all examples of health-enhancing physical activity.

Moderate-intensity physical activity. On an absolute scale, physical activity that is done at 3.0 to 5.9 times the intensity of rest. On a scale relative to an individual's personal capacity, moderate-intensity physical activity is usually a 5 or 6 on a scale of 0 to 10.

Vigorous-intensity physical activity. On an absolute scale, physical activity that is done at 6.0 or more times the intensity of rest. On a scale relative to an individual's personal capacity, vigorous-intensity physical activity is usually a 7 or 8 on a scale of 0 to 10.

Lifestyle activities. This term is frequently used to encompass activities that a person carries out in the course of daily life and that can contribute to sizable energy expenditure. Examples include taking the stairs instead of using the elevator, walking to do errands instead of driving, getting off a bus one stop early, or parking farther away than usual to walk to a destination.

Longitudinal studies. In longitudinal research, scientists observe changes over an extended period of time to establish the time-sequence in which things occur or the effect of a factor over time.

Observational studies. In observational research, scientists observe groups of people to identify characteristics (such as traits and choices) that are associated with disease or health.

Purposeful exercise. A planned physical activity performed with the intention of acquiring fitness or other health benefits. Working out at a gym, swimming, participating in group exercise classes such as aerobics, cycling, running, and sports, like golf and tennis, are all examples.

Randomized Controlled Trial (RCT).

In a typical randomized controlled trial, people are randomly selected to receive either the intervention or a control condition. In a double-blind trial, both the participants and the researchers are “blind” to which person received the intervention until after the results are analyzed.

Risk. Risk is the chance or probability of a particular event happening in a group of people with similar characteristics or traits, compared with not having that characteristic or trait. An individual’s overall risk of having a condition is the cumulative effects of factors that increase the chance of developing the condition (risk factors) as well as factors that decrease the chance of developing the same condition (protective factors).

Risk reduction. Reducing risks for cognitive decline or impairment in the abilities to think, reason, and remember means lowering your chances of experiencing loss in those abilities.

A person’s overall risk may also be reduced by increasing factors that protect against cognitive decline or dementia. Dementia (due to Alzheimer’s disease or another related disorder) is one condition, and cognitive decline (the slowing of thinking and memory in the absence of a major brain disease) is another condition. When scientists study risk reduction strategies for cognitive decline, they are looking for factors that can reduce the risk of impairment to cognitive functions in the population in general. Therefore, some activity or intervention that reduces risk for a particular condition or disease means that a smaller proportion of people who engage in that activity are likely to have the condition or disease. However, risk reduction strategies are not the same as preventing any one individual from getting the condition or suffering from disease. For example, wearing a seatbelt reduced – but did not eliminate – the chance of injuries among people who were involved in automobile accidents, and we now recommend people wear seatbelts while they are driving.

Sedentary lifestyles. This term may be defined as a behavior or lifestyle in which a person expends very little energy, such as short periods of standing, self-care activities, and slow and brief walking. While there is not an internationally accepted standard definition, the experts chose this definition for the purposes of this paper.

Stretching/Flexibility. A health- and performance-related component of physical fitness that is the range of motion possible at a joint. Flexibility is specific to each joint and depends on a number of specific variables, including but not limited to the tightness of specific ligaments and tendons. Flexibility exercises enhance the ability of a joint to move through its full range of motion.

Strength/Resistance. Physical activity, including exercise that increases skeletal muscle strength, power, endurance, and mass. Strength and resistance training are the same thing.



3. Citations to the Public Health Authorities Recommendations Regarding Physical Health

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6. Singapore Health Promotion Board. (2012). *National Physical Activity Guidelines: Professional Guide Physical Activity Guidelines for Adults (19-49 years)* Singapore, Singapore. Pg. 12-15.
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4. Discussion Questions

1. Can physical exercise maintain or enhance cognitive function in people without cognitive impairment as they age? Is there evidence for the following types of exercise:
 - a. Aerobic
 - b. Strength and resistance training
 - c. Stretching and mild activity (i.e. walking)
2. Is there evidence concerning the likely duration and frequency that can result in the greatest cognitive benefit for middle age and older adults with respect to the following types of physical exercise?
 - a. Aerobic
 - b. Strength and resistance training
 - c. Stretching and mild activity
3. What is the evidence that brain function or structure can change after these types of exercise?
4. Is there any evidence that these types of exercise can be used in middle age and older adults as a risk reduction strategy to delay the onset of:
 - a. Cognitive decline
 - b. Alzheimer's disease
 - c. Other dementias
5. Is there evidence for how to motivate middle age and older adults to change their pattern of physical activity? For example:
 - a. Given physical, social and environmental considerations, do you think that healthy, motivated adults can overcome systemic barriers to undertake these types of exercises?
 - b. How do you encourage behavior change with respect to physical activity among middle age and older individuals who are unmotivated? What kind of messages and or activities would impact the unmotivated, and encourage sustained habits of activity?
 - d. Do you know of examples where middle age and older adults have been successfully motivated to exercise who may otherwise have not been inclined "to engage in physical exercise?"
6. How well does the standard framework for evaluating levels of evidence in other medical fields (i.e. cancer and cardiovascular disease) fit within the context of clinical trial data on the impact of physical activity on cognitive performance among middle age and older adults? For example, should long term epidemiological data be more heavily weighted than is the case with respect to diseases such as cancer, since some of the benefits of physical activity may not be measurable within the length of a standard clinical trial setting?

5. Differences, Strengths and Limitations of Two Study Types in Humans

	Epidemiological Studies	Randomized Controlled Trials
PURPOSE	To observe a group of people in their natural surroundings (often over extended periods of time), and to identify personal characteristics, behaviors, and conditions which predict someone's chance of developing a condition or a disease.	To determine, in a controlled setting, whether implementing a change (in behavior, diet, medication, etc.) can definitively lead to a specific outcome. This compares those engaging in an activity with those not engaging in the activity.
EXAMPLE	Researchers who survey and follow women living in Metropolis show that women who run weekly have fewer incidents of heart attack in their 60s.	Researchers at University Medical Center wish to recruit 500 women in their 60s to determine whether having them run weekly can reduce their chance of heart attack during the one year study compared to those who don't run.
STUDY DURATION	Years to decades	Weeks to months, sometimes years
STRENGTHS	<ul style="list-style-type: none"> • Usually larger number of people. • Can take into account influences from many more factors and personal characteristics and disease states. • Can assess many dose levels and durations of behavior. • Can detect slow or cumulative changes over time. • Where observational studies are representative of the population, they have greater external validity which means that the findings can be applied to a wider range of people. 	<ul style="list-style-type: none"> • Helps to prove causal link and to better understand mechanisms. • Randomization can eliminate many competing hypotheses as to why the change actually happened (because confounding factors have an equal probability of occurring in all groups). • Can test whether different dose of the intervention (e.g., exercise frequency, drug dose) can lead to different outcomes. • Uses detailed and objective measurements and assessments.
LIMITATIONS	<ul style="list-style-type: none"> • Does not prove any specific causal link. • May not capture all characteristics which influence health. • Any characteristic may reflect another more important factor (e.g., people who take expensive medications may have better access to health care). • Selective drop-out of those less socially advantaged and less healthy. • Difficult to generalize from one region to another due to differences in diet, environment, healthcare, etc. • Often cannot collect detailed information due to the large numbers of participants and measures. • Expensive to set up and run, especially over long periods. • Some studies rely on self-reported behavior which may be inaccurate. • People who partake in a study to be followed for long periods of time might bias inclusion. 	<ul style="list-style-type: none"> • Usually smaller number of people • While an RCT attempts to control for confounding factors, it may not capture all characteristics which influence health. • The study may be too limited in size or duration to detect subtle effects. • Difficult to test conditions which scientists cannot change (e.g., gender, genetics, past exposure). • Difficult to generalize from one region to another due to differences in diet, environment, healthcare, etc. • In smaller RCTs, outcomes can be biased by accidental inclusion of people who are much more or much less likely to respond to the intervention. • Effects are restricted to defined dose and intervention type. • RCTs usually have very strict inclusion and exclusion criteria so the samples are often unrepresentative and results cannot be as widely generalized. • Attrition rate during the course of the RCT could bias the results. • Outcome reporting bias can influence results in which primary outcomes are changed, introduced or omitted since the original protocol. • Short time frame limits capacity to examine long term interventions which is particularly relevant for lifestyle changes that may lead to small, cumulative effects over years and decades such as physical activity.

6. Disclosure Statement of Potential Financial Conflicts of Interest

All of the twenty-one experts participating in the formulation of this paper were identified as having no financial conflict of interests. Eighteen of the experts who participated in the meeting and contributed to the formulation of the recommendations attested they had no conflicts of interest. Two disclosed potential conflicts of interest involving consultation with pharmaceutical companies or new drug investigations. None of these were relevant to physical exercise, the topic of the meeting, or the recommendations made in this paper. Finally, Professor Anstey declared that the Australian National University is in the process of commercializing a version of an Alzheimer's disease risk tool that Professor Anstey and colleagues have developed, which is currently available freely online and is being used in an online class. The authors are unaware of any affiliations that might be perceived as affecting the objectivity of this paper and recommendations.

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Notes



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