The Manitoba Follow-up Study

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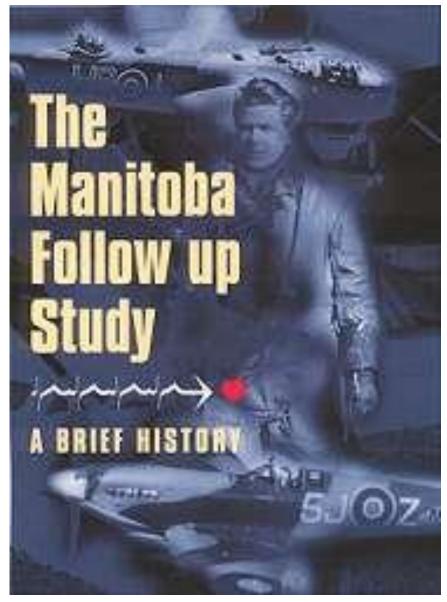


The Manitoba Follow-up Study is currently funded by:

- Research Manitoba
- University of Manitoba
- Donations from Study Members and Their Families

I have no conflict of interest to disclose ... Robert Tate

May 11, 2016



The Manitoba Follow-up Study

- Origin, Design and Conduct of MFUS
- Research Highlights
 - » Cardiovascular Epidemiology
 - » Understanding Successful Aging
- The Study Members
 - » Ownership, Engagement and Support
 - » Perception of Participation and Advice
- Academic Collaboration





FAL Mathewson, MD 1905 - 1994

- Graduate of UM Medical School 1931
- Winnipeg General Hospital physician 1935-1975
- Late 1930s with the Canadian Army
- During WWII Deputy Director of RCAF Medical Services
- Medical Director of Great West Life
- HBC Western Canada historian
- Director MFUS to 1988



TE Cuddy, MD 1930 - 2014

- RCAF, Pilot Officer and Medical Reserve
- Graduate of UM Medical School 1954
- Dr Mathewson's summer student
- Section Head of Cardiology, U of M
- Professor Emeritus and Senior Scholar
- Director MFUS from 1988 to 2001
- Director Emeritus of MFUS

Origin of MFUS

- Initiated by Dr. FAL Mathewson during WWII
- Physical examination of young aircrew recruits during war years
- Survivors contacted between 1946 and 1948
- Housed since 1948 at University of Manitoba



Formation of Cohort

- Cohort sealed July 1, 1948
- 3,983 healthy men
- Mean age 30.1 ± 6.1 years
- 90% were 20 to 39 years of age
- 124 "younger" men were later included at the request of the Department of Transport (DOT)



MFUS Cohort Spans 67 Years

In 1948:

- 3,983 male air recruits
- Mean age 30y
- 90% were 20-39y
- All across Canada
- Free of heart disease

In 2015:

- 298 alive (7.5%)
- Mean age 94y
- 94% are 90y+
- 92% in Canada
- 36% developed IHD



A Prospective Study of Healthy Young Men



Then ...



... Now

Dr. Mathewson's Aim

"Because the suspicion of heart disease, particularly coronary artery disease, may have a far reaching effect upon the individual, it is important to identify beyond any reasonable doubt the clinical significance of those variants that appear in the electrocardiograms of apparently healthy people."

Circulation 21:196-203, 1960



Study Personnel – Early Years

- Medical technician training centre
- Service personnel "posted" to UM Medical School
- Clerical staff for MFUS
- Summer medical students



Medical Examinations

- Height, weight, blood pressure
- General cardiovascular assessment
- Resting 12 lead electrocardiogram
- Member examined by his personal physician
 - » 1948 to 1963 every 5 years
 - » 1963 to 2000 every 3 years
- Yearly "medical update" since 1978
- More frequent examinations by RCAF and DOT



Annual Contact

From 1948 to 1978 ... postcard

- to confirm vital status and maintain address registry Since 1978 ... one page questionnaire
 - address, alternate contact, medical update
 - trigger inter-examination follow-up
 - signed release for information from hospital or physician

Since 1996 ...

contact has been increased to twice yearly

Since 2006 ...

contact has been increased to three times yearly

Periodic Questionnaires

In 1968 and 1974

- Smoking, family history of disease, occupation In 1982 and 1984
 - Physical activity, wartime stress

Beginning 1996, 2000, 2002, 2004, and annually since...

• Successful Aging Questionnaire (SAQ) including mental, physical and social functioning (SF-36) and a narrative reply to "What is YOUR definition of successful aging?"

Beginning 2007, and annually since...

Nutritional risk



Data Collected

Annual Contact

• 181,234 person-years of observation

Medical Examinations

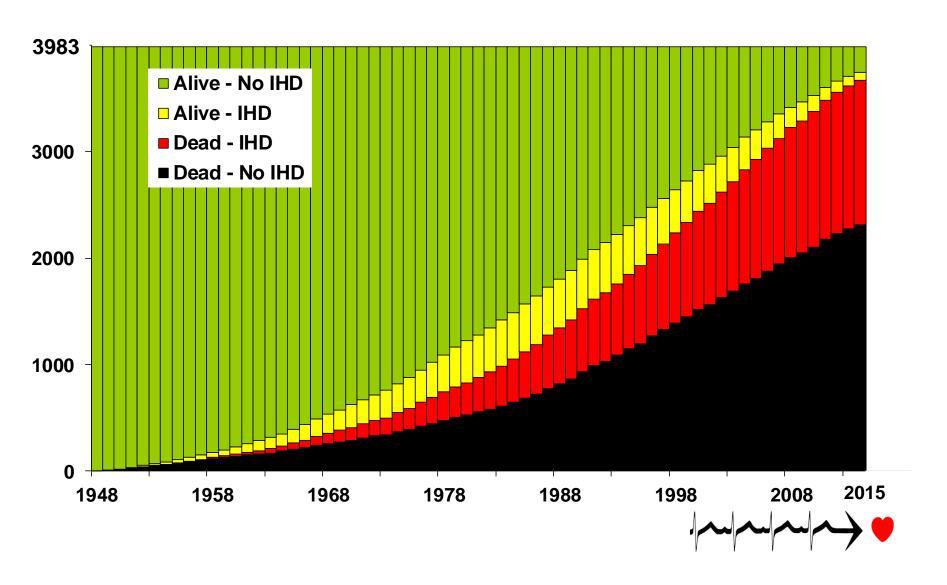
- 74,104 Electrocardiograms
- 98,354 Blood pressure/weight
- 93,890 Clinical entries

Questionnaires

- Smoking, activity, war time stress
- ~10,500 Successful Aging
- ~2,600 Nutritional Risk



MFUS Cohort: 1948 to 2015



Research Findings

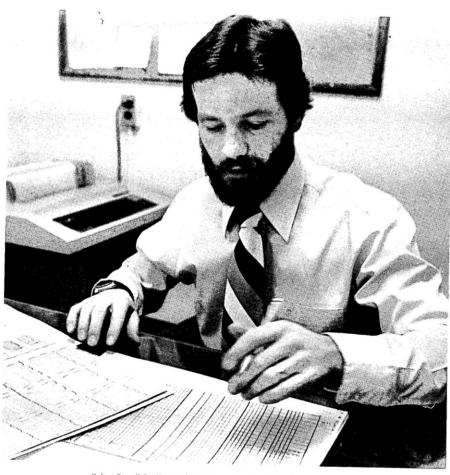


Chronology of Research Reporting

- 1950s Early case series reports, annual reporting
- 1960s First analyses of morbidity and mortality
- 1970s Natural history of EKG abnormalities
- 1980s Relationship of body build and blood pressure to cardiovascular disease and stroke
- 1990s Longitudinal analysis and patterns of chronic disease risk factors
- 2000s Successful Aging, nutrition
- 2010s Successful Aging, perceived control, liver disease, biostatistical methods



Statistician at Work (1979)



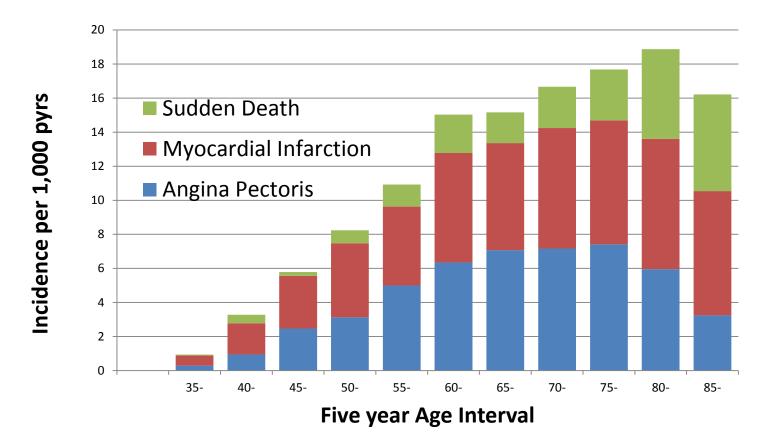
Robert Tate (B.Sc. '73, Mathematics, Statistics) is a research associate to a seven-member medical team conducting cariovascular research. He is responsible for computer programming support and for statistical analysis of data collected over a long term. Prior to joining this troup he completed his M.Sc. (Statistics) at the University of Manitoba.



Cardiovascular Disease



Sixty year Incidence of Ischemic Heart Disease: 1948 to 2008





First Peer-Review Paper from MFUS

(published before I was born)

- The EKGs of 57 young recruits to RCAF were noted to have a prolonged PR Interval (>0.20 sec).
- Etiology and consequence was uncertain.
- After a mean follow-up of 9 years,
 - » there were no deaths, and
 - » only one man had experienced a cardiac event

Adapted from: Mathewson FAL, Taylor WJR. Assoc Life Insur Med Dir America 1952.



Possible Factors Associated with Development of IHD

- "General description" of MFUS experience to 1963
- First 210 deaths and 143 cases of IHD
- Gradient of increased risk found for:
 - » Non specific S-T and/or T-wave changes
 - » Systolic and Diastolic blood pressure
 - » But, not average heart rate or body weight

Adapted from: Mathewson FAL, Brereton DC, Keltie WA, Paul GI. Canadian Med Assoc J 1965.



Body Mass Index and Development of IHD

- After 26-years follow-up, 390 men with IHD
- Gradient of increased risk found for Age, SBP,
 DBP and BMI
- Risk associated with BMI
 - » Greatest for Sudden Cardiac Death
 - » Greater for younger men, compared to older men

Adapted from: Rabkin SW, Mathewson FAL, Hsu PH. Am J Cardiol 1977.



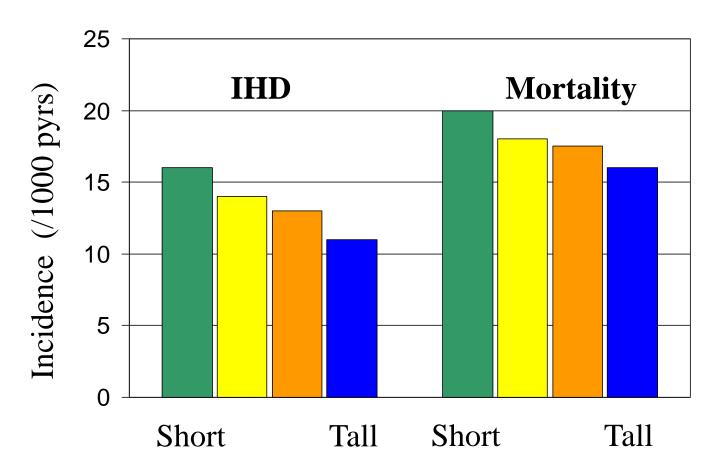
Height as Risk Factor

Body Mass Index (weight/height²)
 is a risk factor for IHD.

- Body weight is associated with IHD
- Might height alone be an independent factor as well?



Height as Risk Factor



Adapted from: Krahn AD, Manfreda J, Tate RB, Mathewson FAL, Cuddy TE. Am J Cardiol 1994.

Natural History of Atrial Fibrillation

Incidence

- » Common rhythm disturbance: 1 in 10 elderly men
- » Can be both persistent and transient
- Risk factors...
 - » Hypertension, obesity
 - » Prior IHD, Non-specific EKG abnormalities
- Prognosis...
 - » 1.3-fold increase in Total Mortality
 - » 2.5-fold increase in Stroke
 - » But, no increase in Myocardial Infarction

Adapted from: Krahn AD, Manfreda J, Tate RB, Mathewson FAL, Cuddy TE. Am J Medicine 1995.

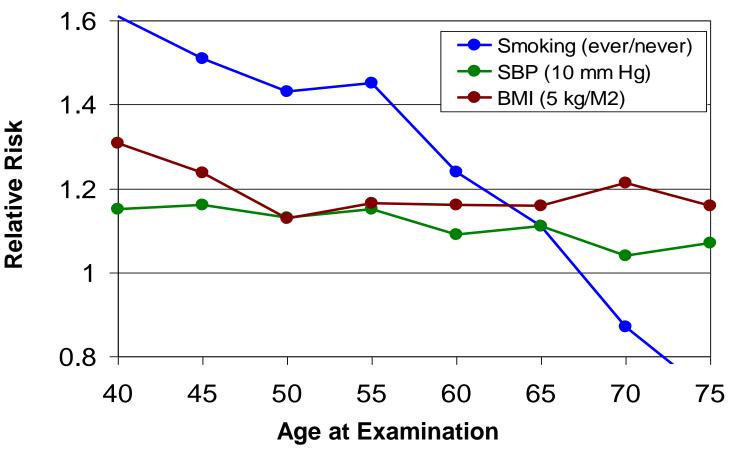


Effects of Aging on Risk Factors for IHD

- Risk factor profiles change with age
- Incidence of IHD increases with age
- What effect might aging have on the relationship between the two?



Relative Risk of IHD by Age



Adapted from: Tate RB, Manfreda J, Cuddy TE. Ann Epidemiol 1998.

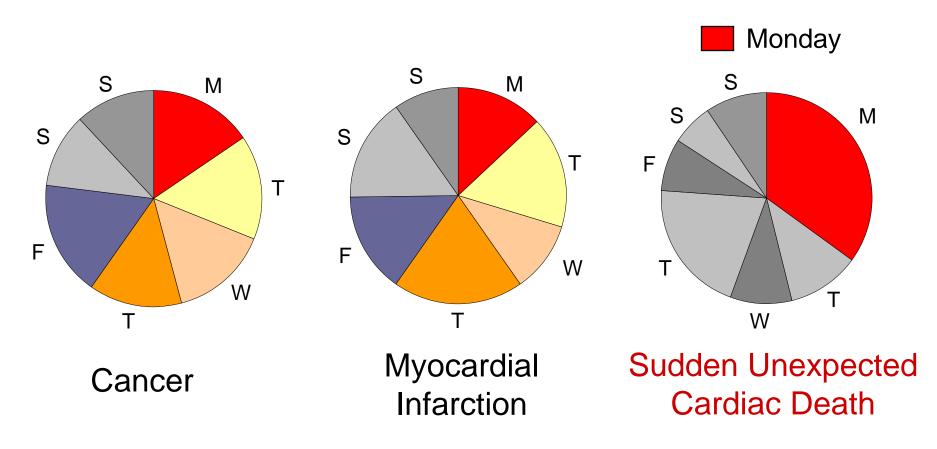


Chronobiology of Sudden Cardiac Death

Are some events, such as heart attacks, cancer diagnosis, death, occurring with equal frequency throughout the week?



MFUS Deaths by Day of Week

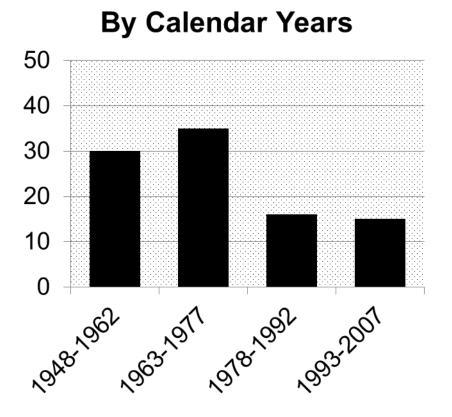


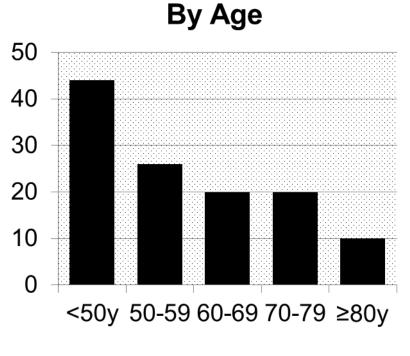
Adapted from: Rabkin SW, Mathewson FAL, Tate RB. JAMA 1980.



Sudden Cardiac Death on Monday - a 60 year update -

Percent of Sudden Cardiac Deaths Occurring on Monday





Tate RB .. unpublished

Healthy and Successful Aging



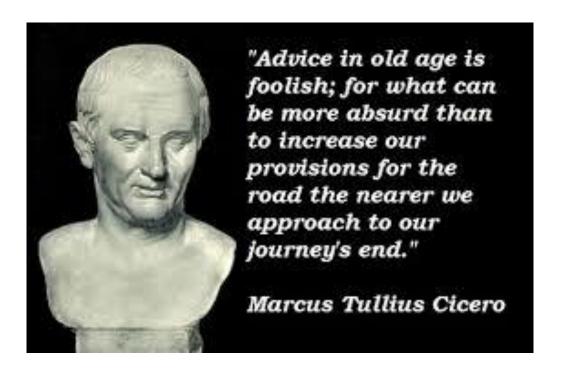
Expanding MFUS Focus

- ... in late 1990s from research based on EKGs, and risk factors for cardiovascular disease, including heart disease, stroke and mortality.
- Today 13% of Canadians are over age 65 years, by 2040, 25% will be over 65 years.
- Move from studying not only chronic disease to quality of life of older Canadian men.



Marcus Tullius Cicero

(Born 106 BC in Rome, Assassinated 43 BC in Formia)



Cicero suggested that in old age the individual should focus on the mind, and not be distracted by bodily needs....

"Nothing [is] more directly destructive to the dignity of man than the pursuit of bodily pleasure."



North American History of Aging Research

- USA 1944 American Social Science Research
 Council "Committee on Social Adjustment to Old Age"
- Havighurst (1961) "Currently, there are essentially 2 gross theoretical models of successful aging: the activity theory emphasizing the maintenance of the activities and attitudes of middle age, and the disengagement theory, essentially withdraw from active life."
- Fries (1980) compression of morbidity, a goal to live life to the fullest, free of disability as long as possible, and decline quickly to death.
- Baltes and Baltes (1990) SOC model selection, optimization, compensation. (*** pictorial example to follow ***)
- Rowe and Kahn (1987,1998) intersection of three concepts –
 1) low physical disease/disability, 2) high cognitive functioning, 3) active engagement with life

Mr F (age 95) in Victoria









Understanding "Successful Aging"

- "Successful Aging" is a desirable state-of-being in later life, indeed throughout life
- Widely used concept, but no universal definition
- Successful Aging has many dimensions:
 Health, active engagement with life, vitality, resilience, adaptation and acceptance, spirituality, happiness
- For resource planning, we must understand the population's views about "Successful Aging"



Our First Successful Aging Questionnaire (SAQ)

- MFUS survey developed in spring of 1996
- 1,821 of 2,043 (89%) MFUS members responded after 3 mailings
- Living arrangements, social activities, activity limitations, physical/mental functioning (SF-36)
- Content analysis of narrative responses to: "What is *your* definition of successful aging?"



First Results in 1996

- 20 different themes of SA were provided:
 - » 30% ... Health / disease
 - » 28% ... Happiness / satisfying life
 - » 20% ... Keeping active physically
 - » 19% ... Positive outlook / attitude
 - » 19% ... Family / friends
 - » 17% ... Independence
 - » 10% ... Spirituality / growing old gracefully
- Life satisfaction, self-rated health, and activity limitations related to inclusion/omission of specific themes in a definition

Why might individual definitions of SA be important?

- Over 6 years, from 1996 to 2002, 472 (26%) of the 1,821 respondents to the first SAQ, died.
- Four themes from definitions of SA were significantly associated with an increased, i.e. better, survival rate.



Some SA themes lead to better survival over 6 years... (APHA 2003)

Theme in SA Definition:	Age Adjusted Relative Survival (95% CI):
Keeping physically active	1.46 (1.12, 1.89)
Contentment	2.26 (1.01, 5.05)
Being useful, volunteering	1.84 (1.10, 3.09)
Having a positive outlook	1.32 (1.02, 1.70)



Successful Aging Questionnaire

Fifteen SAQs have been mailed since 1996. Annual response rates vary from 75% to 89%.

Core questions include:

- Living arrangements, marital status, residence
- Mental, physical and social functioning (SF-36)
- Self-rated health and life satisfaction
- Participation in leisure time activities
- Basic and instrumental activities of daily living
- "What is YOUR definition of successful aging?"
- "Would YOU say you have aged successfully?"



SAQ add-on components

1996: Occupation, retirement

2000: Diet and nutrition

2002: What is 'being old'? Are you old?

2004: Weight recall, long-term effects of WWII

2005: Changes in diet, driver and pilot licenses

2006: Care-giving, income adequacy

2007: How and why has your SA definition changed?

2008-2014: Importance of items to determine QoL

2010: Diet and nutrition, memory

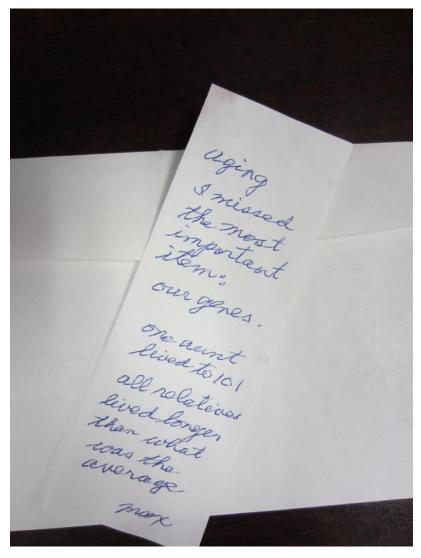
2011-2012: Psychological control

2013: Advice for Canadian Forces, VAC and CLSA

2014: Personal challenges for future

2015: Frailty

Arrived in the mail ... from Max





Year of Survey	Number of surveys mailed (% returned)	Number of surveys returned with SA definition	Age in years mean ± st dev
1996	2,043 (87%)	1,745	76.6 ± 3.7
2000	1,661 (81%)	1,319	80.2 ± 3.4
2002	1,476 (81%)	1,153	82.0 ± 3.3
2004	1,215 (74%)	870	83.8 ± 3.2
2005	1,112 (80%)	860	84.6 ± 3.0
2006	1,001 (84%)	807	85.6 ± 3.1
2007	881 (80%)	680	86.3 ± 3.0
2008	757 (81%)	589	87.2 ± 2.9
2009	667 (83%)	522	88.0 ± 2.8
2010	581 (83%)	450	88.8 ± 2.8
2011	467 (81%)	360	89.7 ± 2.9
2012	387 (87%)	298	90.7 ± 3.0
2013	330 (79%)	245	91.4 ± 3.0



Year of Survey	Married %	Aged Successfully? % Yes	Self-rated health % excellent	Life satisfaction % excellent
1996	83	88	31	38
2000	79	84	25	34
2002	77	87	22	31
2004	74	89	14	27
2005	71	83	12	18
2006	69	86	12	17
2007	66	80	13	16
2008	67	82	12	18
2009	66	77	11	16
2010	66	77	10	16
2011	65	84	12	15
2012	62	80	11	13
2013	60	76	12	16

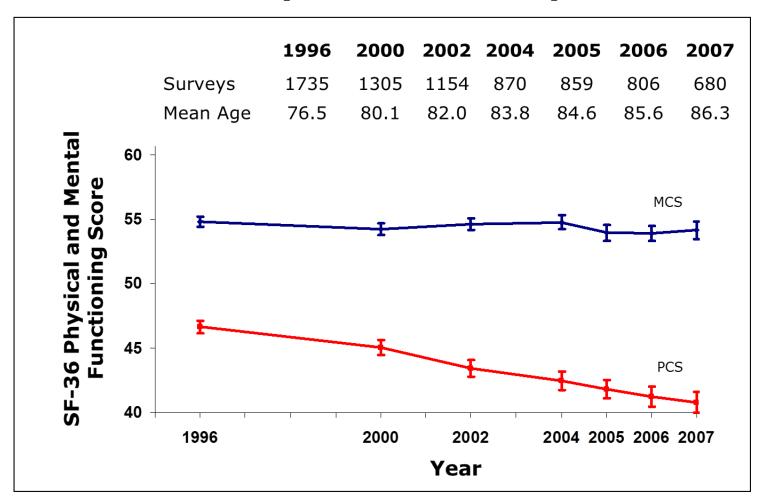


Mr D's (87y) SAQ 2015 response





Mean MCS and PCS (with 95% CI) by Year of Survey





Multiple Linear Regression Coefficients for Binary SA Themes in Models of PCS and MCS (GSA 2009)

Theme in Definition of Successful Aging	Mental Component Score	Physical Component Score
	Coefficient ± SE	Coefficient ± SE
Mental Health – Attitude	1.06 ± 0.20	-
Acceptance/Coping	1.03 ± 0.32	-0.63 ± 0.33
Mental Activity	1.03 ± 0.28	-
Adaptation	0.93 ± 0.26	0.64 ± 0.32
Life Experience	0.87 ± 0.43	1.35 ± 0.45
Mental Health – Happiness	0.82 ± 0.20	-
Having Interests	0.70 ± 0.20	0.72 ± 0.22
Physical Activity	0.58 ± 0.24	1.09 ± 0.25
Independence	0.55 ± 0.20	-



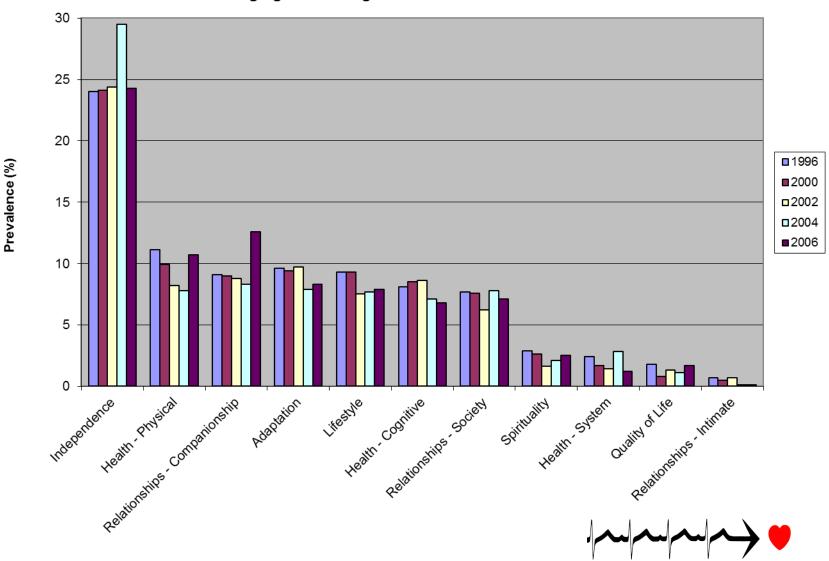
Our SA coding manual...

(The Gerontologist 2003, Can J Aging 2009, IJAHD 2013)

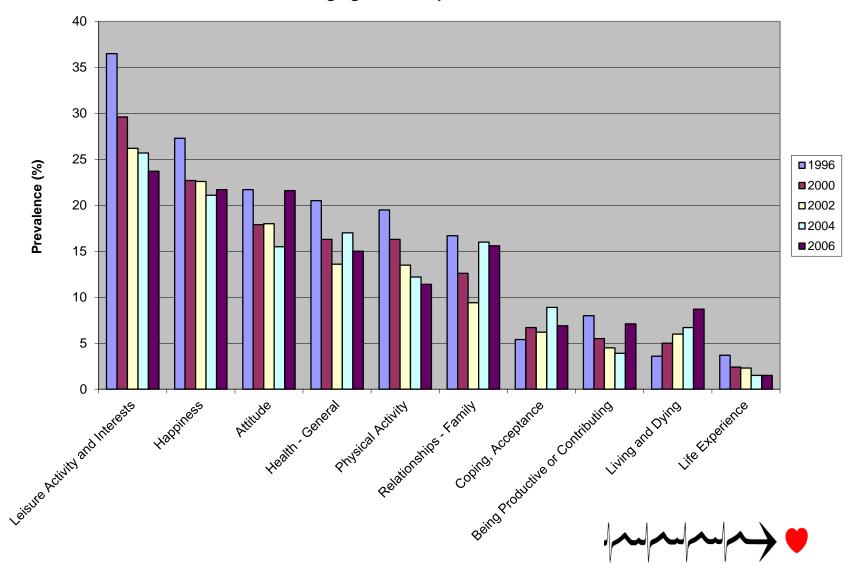
- The 1996 SAQ narratives identified 20 SA themes
- Expanded to 86 themes
- The 86 themes can be easily grouped into 21 theme categories with multiple themes
 (e.g. Independence category contains 8 themes)
- Hired and trained a team of 6 summer students in 2011 to recode SAQs



Themes of Successful Aging with no significant linear trend over Time: 1996 to 2006



Themes of Successful Aging with Unequal Prevalence over Time: 1996 to 2006



Repeatability of Themes of SA: 1996 to 2006 (Odds Ratios with 99%CI)

Odds Ratio 1.0 to 3.0	Odds Ratio 3.0 to 5.0	Odds Ratio > 5.0
Happiness 1.9 (1.6,2.4)	Coping, Adjustment, Acceptance 3.1 (2.0,4.9)	Life Experience 7.7 (3.5,16.7)
Attitude 2.0 (1.6,2.6)	Lifestyle 3.3 (2.2,4.8)	Relationships – Intimate 10.4 (0.7,160)
Independence 2.1 (1.7,2.7)	Relationships – Society 3.3 (2.2,5.0)	Quality of Life 19.9 (6.7,59.3)
Health – Physical 2.3 (1.6,3.3)	Physical Activity 3.4 (2.6,4.4)	Spirituality 24.1 (11.8,49.2)
Health – Cognitive 2.3 (1.5,3.5)	Living and Dying 3.5 (2.1,5.9)	
Relationships – Companionship 2.4 (1.7,3.5)	Relationships – Family 4.2 (3.2,5.7)	
Adaptation 2.4 (1.7,3.6)	Health – System 4.6 (1.7,12.6)	
Leisure Activity and Interests 2.5 (2.0,3.0)	Being Productive, Contributing 4.9 (3.0,7.8)	
Health – General 2.7 (2.1,3.5)		

In Summary, the MFUS view of SA is ...

- Earlier work explored SA as a label, and a goal to strive for.
- Problems arise with a clinician imposed definition of SA.
 - » Who decides if I've "aged successfully?"
 - » If someone tells me I haven't "aged successfully", have I "failed"?
 - » Clinical criteria tend to underestimate success and mislabel individuals who self-identify as having aged successfully.
- Successful aging has many dimensions ... and must be defined by the individual.
- Distributions of SA themes are valuable for planning at the community or population level, but be careful with imposing themes at the individual level.



What we have learned about SA from the MFUS men...

• SA as a **predictor**

* themes of SA predict mortality, mental and physical functioning.

• SA as an outcome

» individual characteristics predict themes of SA.

• SA as a dynamic process

- » although SA themes may change over time, many are highly repeatable at an individual level.
- » an individual may transition "in and out" of self-assessed SA.



Current SA Research at MFUS

- Distinguish between "means" and "ends" of SA in a man's definition.
- Characterization of individuals whose themes change and do not change over time.
- What events in a man's life trigger a change in his definition of SA.
- SA themes related to long-term survival and remaining in the community.



Meet a few Study Members



Mr. H in Guelph (age 89) "Some of my recent creations. P.S. They are for sale."



JUSTIFIED FORCE SIU clears officers in Taser, rubber bullet use to bring down crazed man with knife A3

HAMILTON SPECTATOR

'A very happy man with his lot in life' is how Ralph Connor, 90, is described by the director of the Manitoba Followup Study. Read about the former RCAF pilot and the study that's been going on for nearly 70 years on A6

Ralph Connor: a study in good health

Disciplined lifestyle of ex-airman has been followed for 70 years

MARK MCNEIL

The Hamilton Spectator

Ralph Connor is a man with a lot of self-discipline.

He's 90 years old, with a bad hip that's scheduled for surgery, but still goes to the YMCA at 5 a.m. three times a week to work out with his buddies.

It's something he's been doing for

He's absolutely convinced his exercise regimen - incorporating circuit training and swimming, among other things - along with good genes and a generally healthy diet explain his excellent cardiovascular health and longevity.

And he has some numbers to back that up.

Nearly 70 years ago, he signed up for a cardiovascular disease and aging study of Royal Canadian Air Force airmen who were moving into civilian life after the Second World War. The ongoing research project has turned out to be the longest-running study of cardiovascular disease and aging in Canada.

The study started with 3,983 men. Today, 350 are still alive.

"I realized a long time ago that if I didn't work out early in the morning, it wouldn't get done," says the retired insurance broker, who trained pilots with the RCAF during the war.

He says keeping in shape makes him feel better and has allowed him to do things - until recently, before his hip gave him trouble — such as climb onto the roof of his two-storey house and pick acorns out of the eavestrough. He was 89 the last time he did that.

"He's at the top end, that's for sure," says Robert Tate, director of the Manitoba Followup Study, as it is called. "Mr. Connor is in an elite group that has survived to 90 years old. He is a very happy man with his lot in life. He continues to participate in a lot of activities that bring him pleasure and bring his community pleasure, I suspect."

The research effort was the brain child of Dr. F.A.L. Mathewson, a doctor with a specialty in cardiology, who evaluated the fitness of thousands of recruits for the RCAF during the war.

After the war ended, Mathewson - with assistance from the Canadian military and the University of Manitoba - decided to continue to track the cardiovascular health of the airmen. They had such a tremendous amount of baseline data that it made sense to build on it for a long-term study.



Ralph Connor: 'a happy man'

Mathewson, who died in the 1990s, was particularly interested in seeing whether electrocardiogram results that showed slight abnormalities early in life pointed to more serious car-

diovascular problems later on, something the study would eventually show to be the case.

Tate says the study also found that 35 per cent of the men deemed healthy in the 1940s would develop cardiovascular disease later on. That's about the national average.

Smoking and obesity tended to go hand-in-hand with cardiovascular problems among respondents in their 40s or 50s. But if the problem hadn't shown up by then, the person was no more likely to have cardiovascular disease at an older age than their non-smoking, more physically fit colleagues.

"As expected, people in younger ages who smoke have a greater risk of heart disease later into the future but that risk diminishes with age ... the magnitude of the effect of smoking in a younger man is much greater than ... in an older man," Tate said. "And the same is true with obesity."

Tate says in more recent years the study has evolved into focusing more on what is being called "successful aging" - the goal of finding physical, mental and social well-being in older age.

"It's truly a unique opportunity to look at issues related to older men's lives ... We feel that it is a concept defined at an individual level."

For his part, Connor feels the study is very important, so much so that when funding problems developed many years ago, he put in his own money to help out. Each year, he sends \$150 to keep it going.

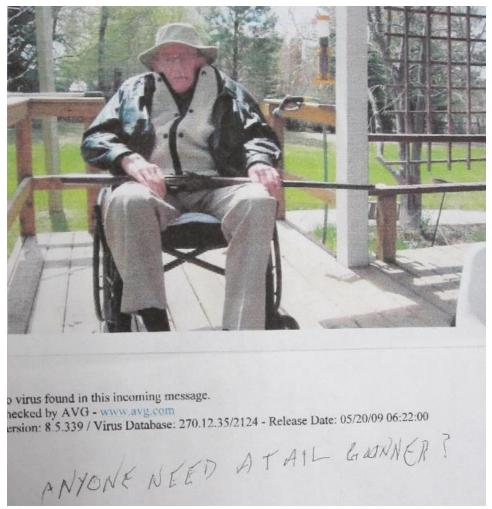
For the 50th anniversary, he travelled to Manitoba, at his own expense, to take part in a celebration held there for participants.

More recently he celebrated his 90th birthday at, you guessed it, the Y. A room was booked, his buddies were invited. They had cake and all the usual.

Did he work out that day? "Oh yeah, of course," he said.

mmcneil@thespec.com 905-526-4687 | @Markatthespec

Mr. B from Rocky Mountain House (age 91) This RCAF Veteran, says it all...



Funding a 67 year Study



Funding: 1946-1983

- Royal Canadian Air Force
- National Research Council of Canada
- Medical Research Council (1961-65)
- Defense Research Board (1962-74)
- Canadian Life Insurance Assoc (1965-75)
- Health and Welfare Canada (1965-83)



Funding: 1984-2000

- 1983 H&W recommend termination of data collection with a contingency to "wind down"
- Study members say "NO"
- MFUS established as a registered charity
- Members form "MFUS-2000" and contribute 75% of operating costs through donations
- Short term pledges obtained from insurance companies, Wartime Pilot and Observers Association, Royal Canadian Legion



Funding: 2001-

- Fewer study members with retirement incomes lead to decline in member contributions
- Veterans Affairs Canada: 2001
- MHRC operating grant to update data systems and enhance follow-up procedures: 2001-2003
- CIHR programmatic grant with renewals: 2003-2011
- Co-investigator funding, local foundations: 2011-2013
- Faculty of Medicine UM: 2014-2015
- Research Manitoba\College of Medicine: 2015-2016
- Continued donations from members and families



Opinions and Advice from MFUS Members ..

Short questionnaires were sent in 2003, 2010 and 2014 to ask members' opinions concerning their participation with this long-term study

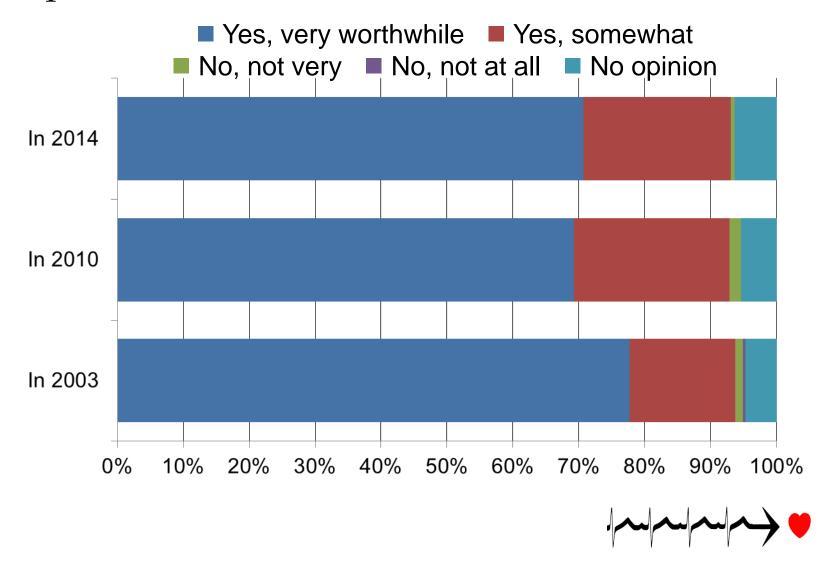


What effect do you think participating in World War II has had on your overall health and well-being? (870 respondents in 2004)

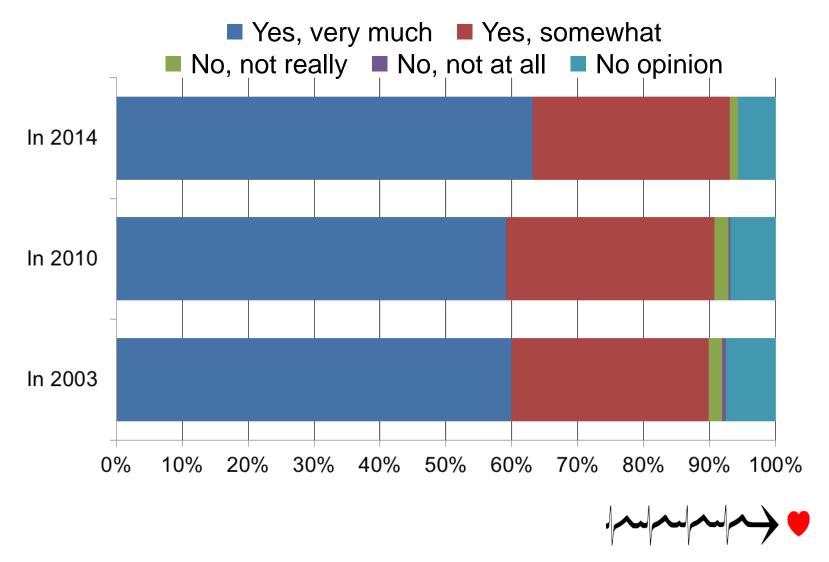




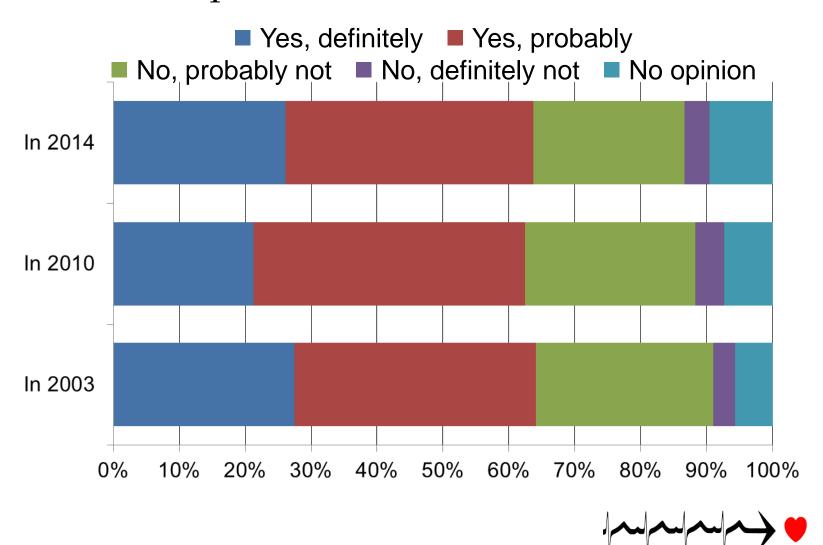
1. Do you feel the time, effort and support you have provided to MFUS have been worthwhile?



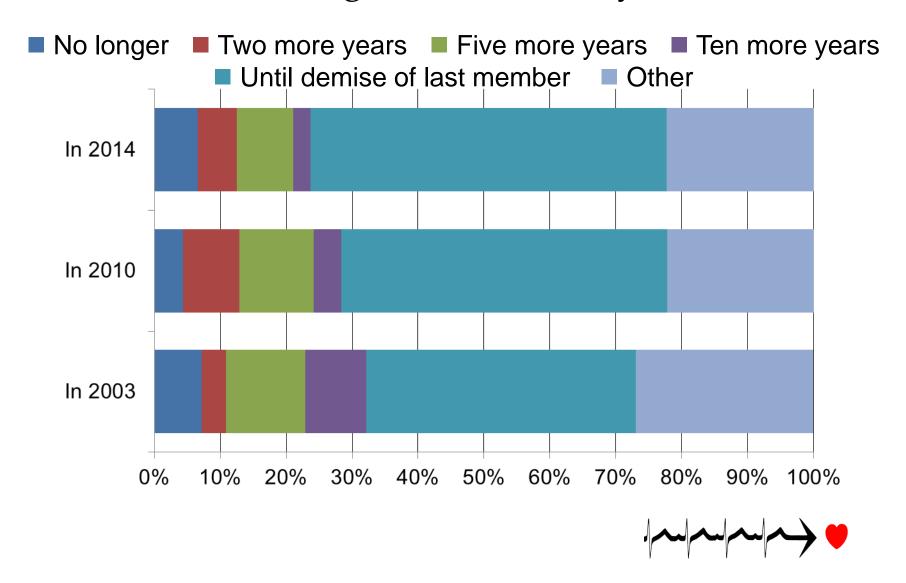
2. Do you feel the results of MFUS have contributed to society's better understanding of human health?



3. Do you feel that participating in this study has had an impact on YOUR OWN HEALTH?



4. How much longer do you think MFUS should continue collecting data from study members?



Value of MFUS

- Healthy outlook of members
- Research contributions to medicine
 - Extends world knowledge concerning heart disease
 - Provides new knowledge in understanding aging
 - First hand research experience for graduate students, medical residents and research trainees
- Database for research and teaching
- Collaboration with other investigators



U Manitoba Co-investigators

- Dr Phil St. John Functional trajectories and frailty
- Dr Christina Lengyel Nutrition of Older Adults
- Dr Audrey Swift Psychology of Perceived Control
- Dr Ruth Barclay Response Shift and QoL
- Dr Depeng Jiang Person-oriented methodologies
- Dr Julia Uhanova MetS and Liver Disease
- Dr Mahmoud Torabi Longitudinal data analysis



3 MFUS Directors through 67 years

- Photo taken at Dr Mathewson's home celebrating the presentation of the Wilbur R.
 Franks Award for "Dedicated Contribution to Aerospace Medical Matters in Canada" March 10, 1992
- The long-term likelihood of success of any cohort study is increased by the dedication of study participants and continuity of committed staff.

