Summer Program in Aging

Canadian Frailty Network

John Muscedere
Scientific Director
Canadian Frailty Network

Canadian Frailty Network | Réseau canadien des soins aux personnes fragilisées

What is Canadian Frailty Network (CFN)

- National non-profit network funded by Networks of Centres of Excellence
- NCE supported by CIHR, SSHRC, NSERC, Industry Canada, Health Canada
- TVN launched in July 2012
- 5-year funding

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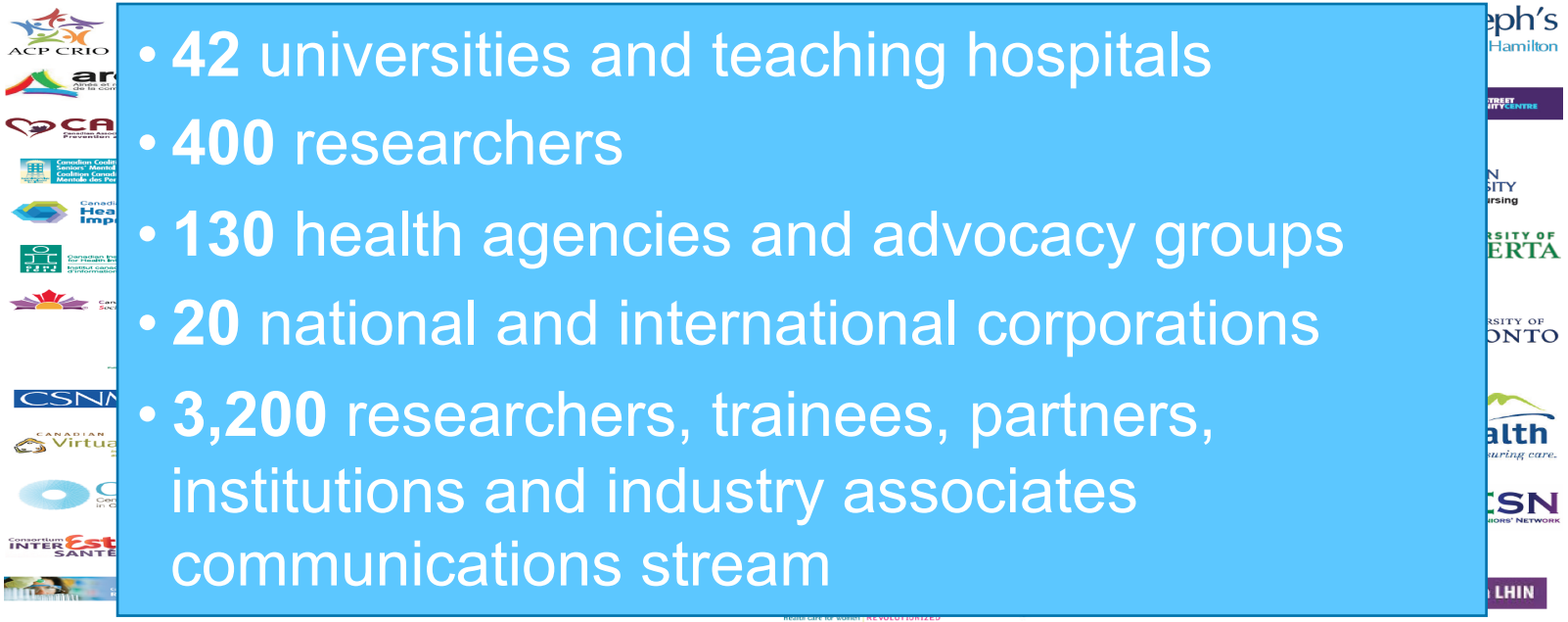
Queen's University

RCE NCE
Réseaux de centres d'excellence du Canada | Networks of Centres of Excellence of Canada

Canadian Frailty Network



- **42** universities and teaching hospitals
- **400** researchers
- **130** health agencies and advocacy groups
- **20** national and international corporations
- **3,200** researchers, trainees, partners, institutions and industry associates communications stream

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CFN's mission as an NCE is to…

Develop, evaluate and disseminate knowledge on health care for the frail elderly, their families and caregivers

such that…

"Frail elderly Canadians receive the right care, in the right setting, at the right time"

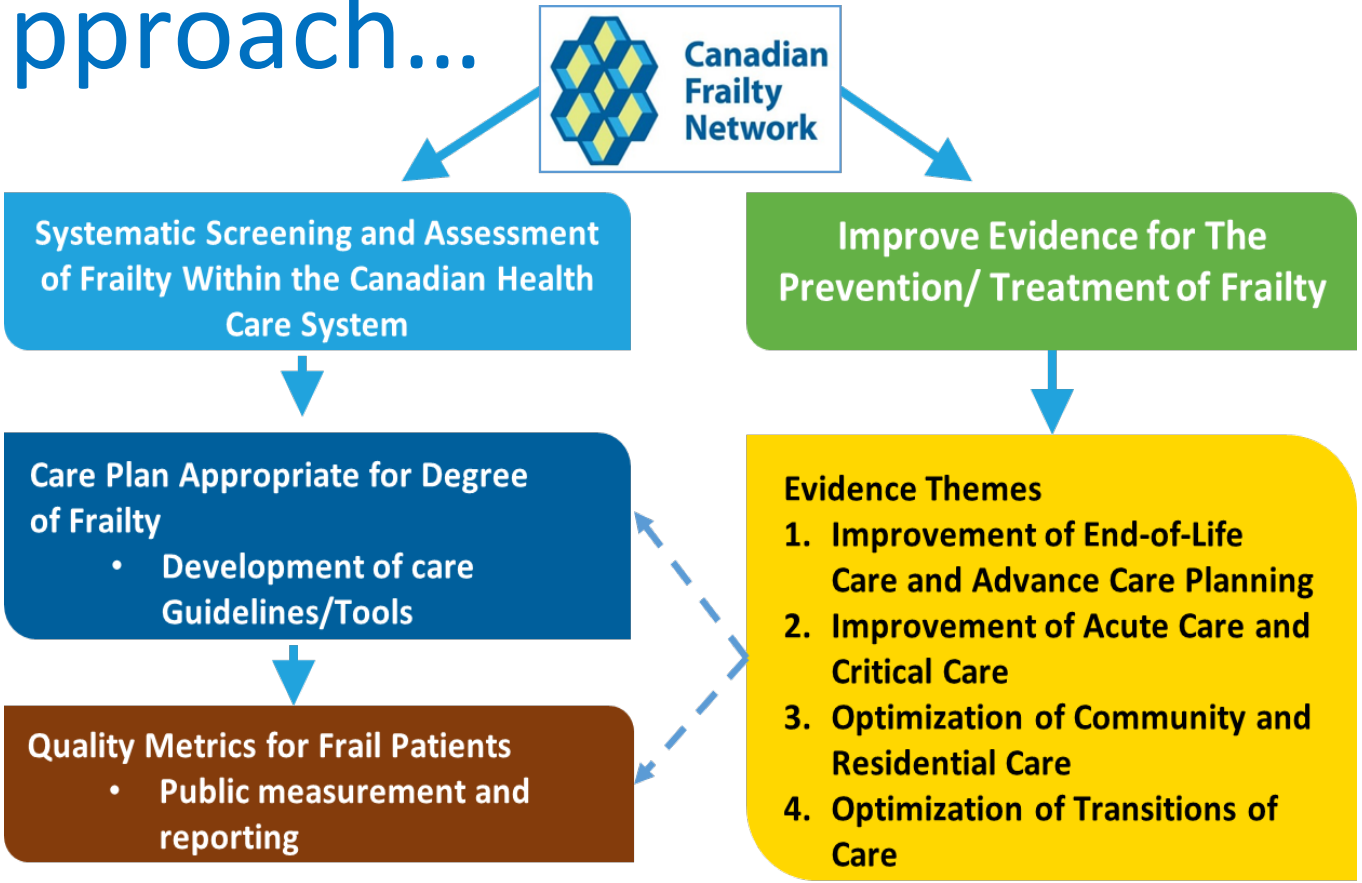
CFN's focus

- Frail elderly Canadians where there are questions on which therapies to apply to improve survival and quality of life or quality of death, including end-of-life care
- Therapies include the spectrum from life support modalities to methods of care to systems of care.
- All settings spanning from home/community care to acute/critical care including transitions of care.

CFN Components

- Research Program
- Training of Highly Qualified Personnel (HQP)
- Knowledge Mobilization
  - Giving voice to frail elderly Canadians
  - Frailty assessment in all settings of care
- Partnerships and Network Expansion

Our approach…



Frailty in the health care system matters…

- It is under-recognized and its impact is under-appreciated
- The healthcare system is organized around single disease, single organ dysfunction
- The healthcare system has not taken into account the wishes of those with frailty or their caregivers
- Evidence generated from studying fit people may not apply

Why frailty assessment matters (2)

"You can't manage what you don't measure".

- Serves as catalyst for innovative care solutions/ interventions that could:
  - Improve health, quality of life of older people and caregivers
  - Delay disability and slow progression of disease
  - Avoid unnecessary hospitalization, institutional care
  - More efficiently use resources, skills, technology; increase sustainability of health and care systems

Research Program

Figure 2: Implementation vs. Observational Studies within CFN

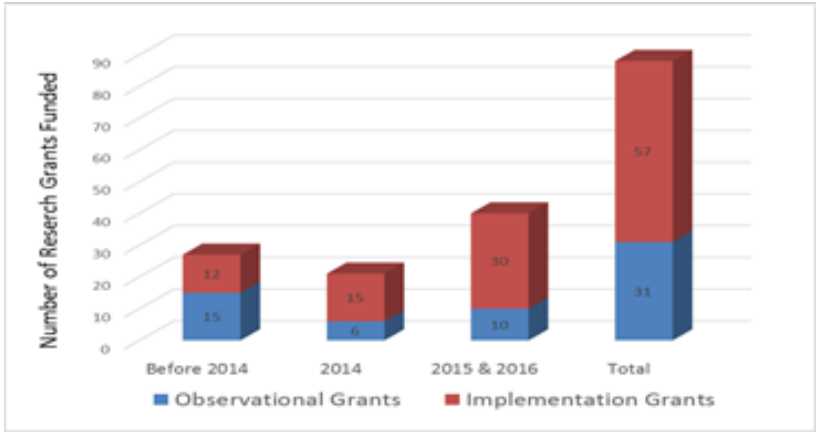
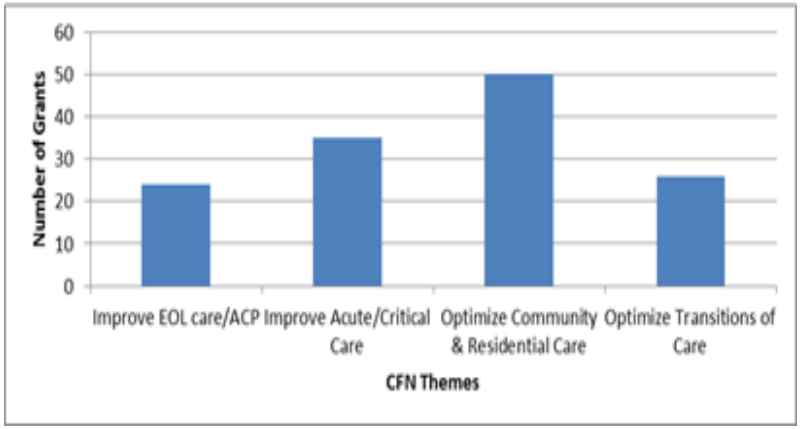


Figure 3: Number of grants by theme. Some grants cross multiple themes and hence the total number is greater than total number of CFN grants (88)



Total of 88 research Proposals funded to present

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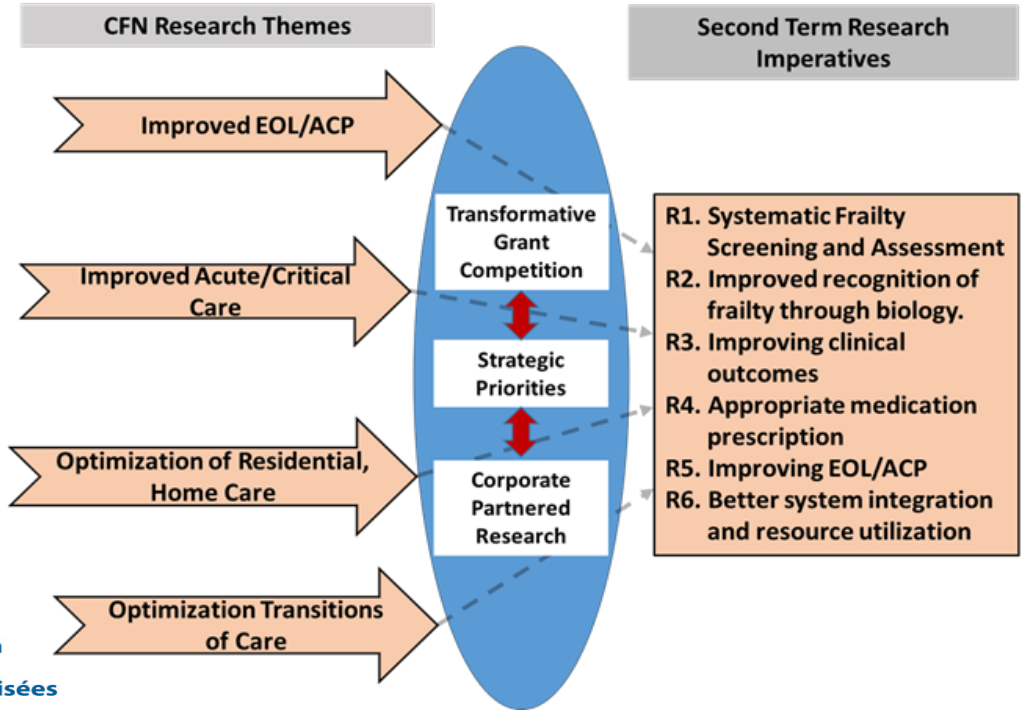
Research Program- future

Figure 7.3.1.2 – Research Imperatives for the second term. An integration of research themes, strategic priorities, competitive research competitions and partnership opportunities.



Knowledge Mobilization

- **Engage frail elderly and family/caregivers**
  - Design of research that informs their care
  - Determining their involvement in health care system
    - How the system is managed, policy advocacy and their role as health consumers
- **Informed by best evidence**
  - Published literature
  - Expert opinions of patient/citizen advocates, researchers, health care providers, administrators

Training Program

- Summer Student Awards
    - Undergraduate- 50 awards
- Trainees sponsored through research grants
    - > 200 trainees
- Inter-disciplinary Fellowship Program
    - 42 Fellows

Future state for frailty…

- Every frail person has an appropriate care plan commensurate with their stage on the frailty continuum
- Care plans are evidence based and regularly updated with new high quality evidence
- Frailty data is readily available to inform research, health system administration and policy
- Delivery of care is tracked through quality indicators

Questions?

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Overview of Frailty

John Muscedere
Scientific Director
Canadian Frailty Network

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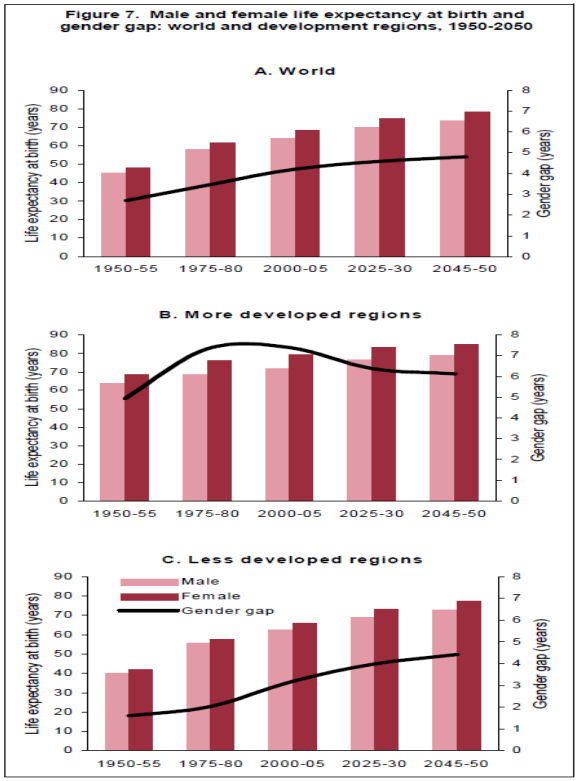
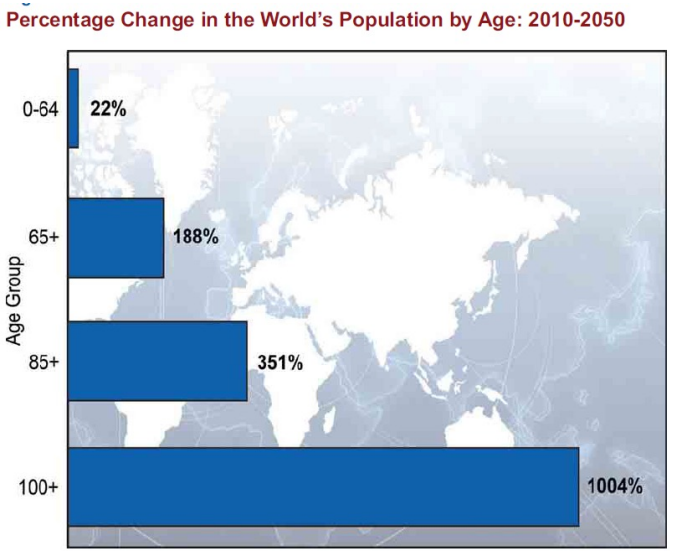
This Presentation

- Definition
  - Concept
  - Syndrome vs. State
  - Biology of Frailty
- Clinical aspects
  - Impact on outcomes
  - Can we improve on outcomes?
- Way forward

Aging and the global perspective





Sources: United Nations:
World *Population Ageing: 1950-2050, 2001*
World Population ***Prospects: The 2010 Revision***

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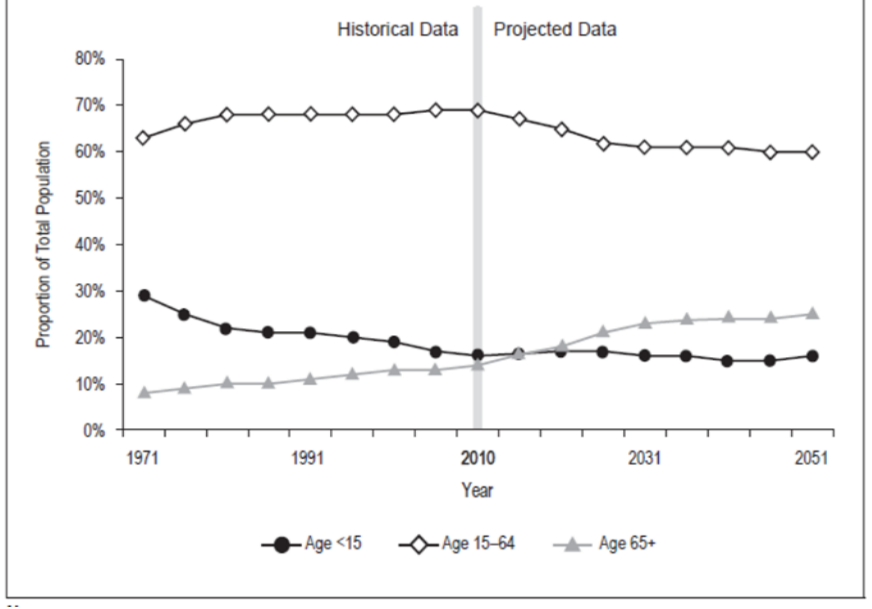
Aging in Canada

- Proportion age 65+ increasing
- Older (age 85+) growing rapidly
- Present: 4.46 working adults for every 1 senior
- Future: 2.84 working adults for every 1 senior (by 2025)

Figure 1: Composition of the Population, by Age, Canada, 1971 to 2051



Source: Canadian Institute for Health Information

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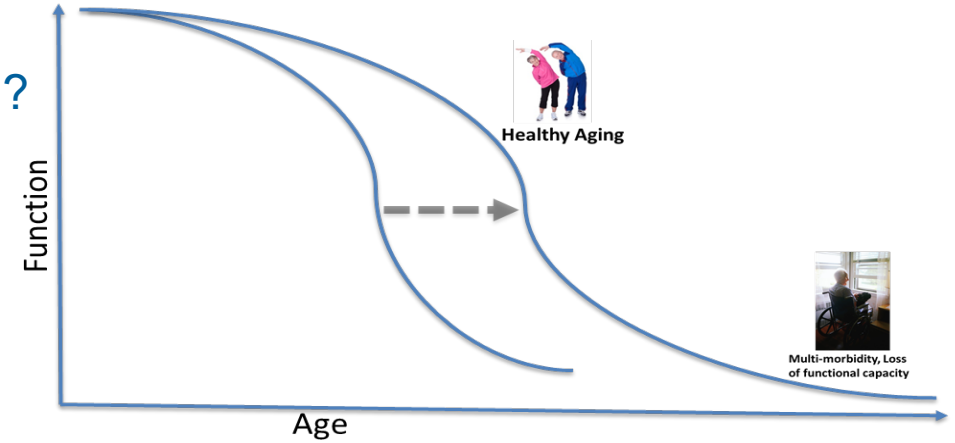
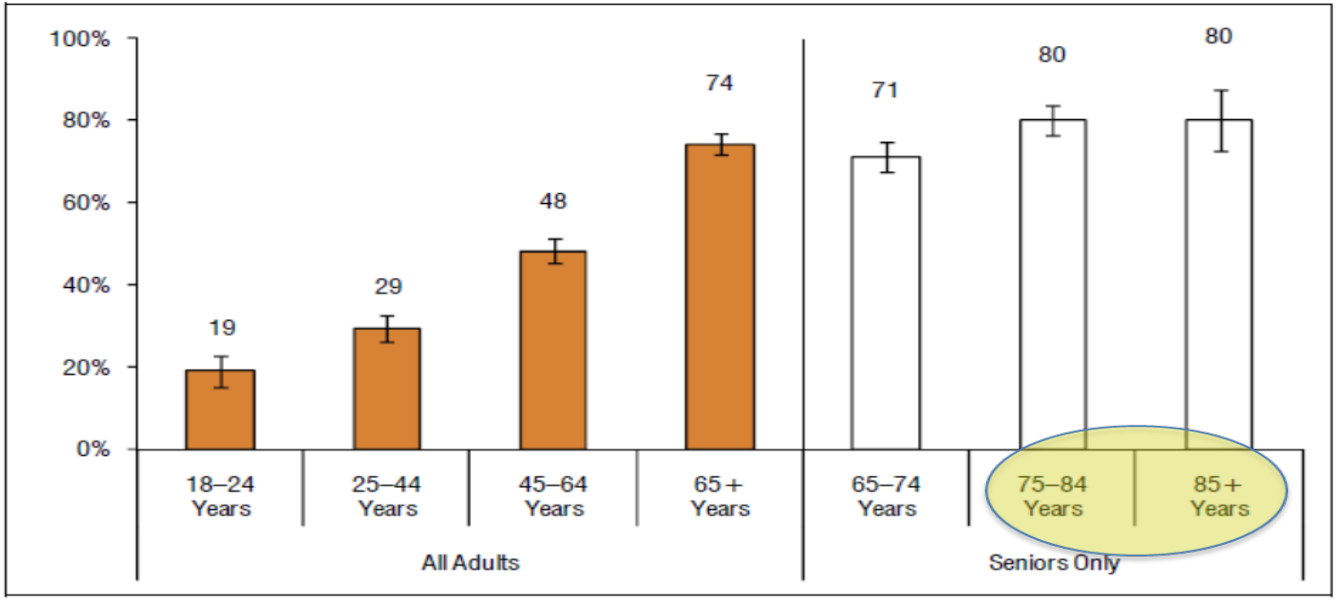
Shift in the aging curve

- Where should our efforts be focused?
- Where is the greatest need?
- Who are the most vulnerable and highest risk?
- How can we ensure that the health system is sustainable?



Medical conditions with age

Figure 3: Percentage of Adults Who Reported Having at Least 1 of 11 Chronic Conditions, by Age Group, Canada (Crude Estimates)



Source: Canadian Institute of Health Information

Concept of risk…

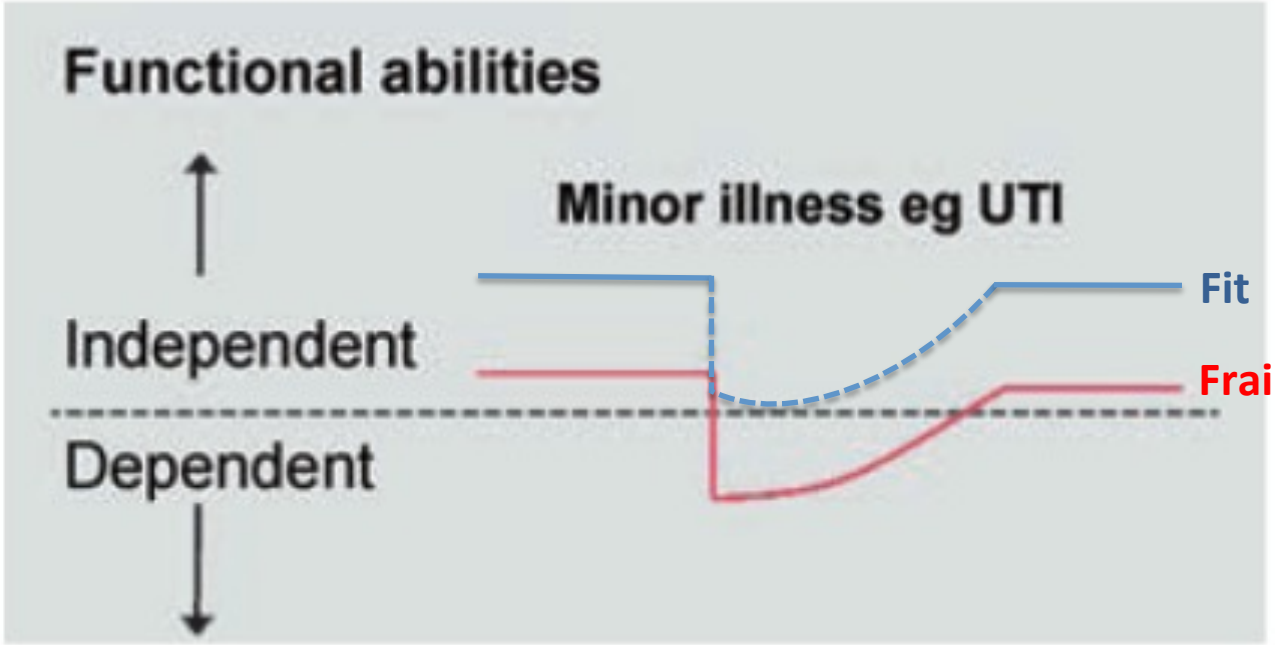
- Not all aging is the same
- Some have increased risk over others of the same age for poor outcomes, mortality
- Lack of reserve
- Concept of frailty

Frailty definition…

- Frailty is defined as a state of increased vulnerability resulting from reduced physiological reserve and loss of function across multiple systems reducing the ability to cope with normal or minor stressors which can cause rapid and dramatic changes in health.

Xue Q. (2012). The Frailty Syndrome: Definition and Natural History Clin Geriatr Med. 27: 1.
Clegg A, Young J. (2011). The frailty syndrome. Clinical Medicine 11: 72.
Walston J et al. (2006). Research Agenda for Frailty in Older Adults: J Am Geriatr Soc 54:991.

Impact of stressors…



Clegg A, Young J. (2011). The frailty syndrome. Clinical Medicine 11: 72.- Modified

Frailty – State vs. Syndrome…

- Syndrome – Phenotype: Fried et al
  - Weakness (grip strength)
  - weight loss (>10 lbs past year)
  - Slow walking speed
  - Inactivity
  - Exhaustion (self-reported)

Frail: 3 or >
Pre-Frail: 1 or 2
Non-Frail: None

- State – Acquired deficits: Rockwood et al

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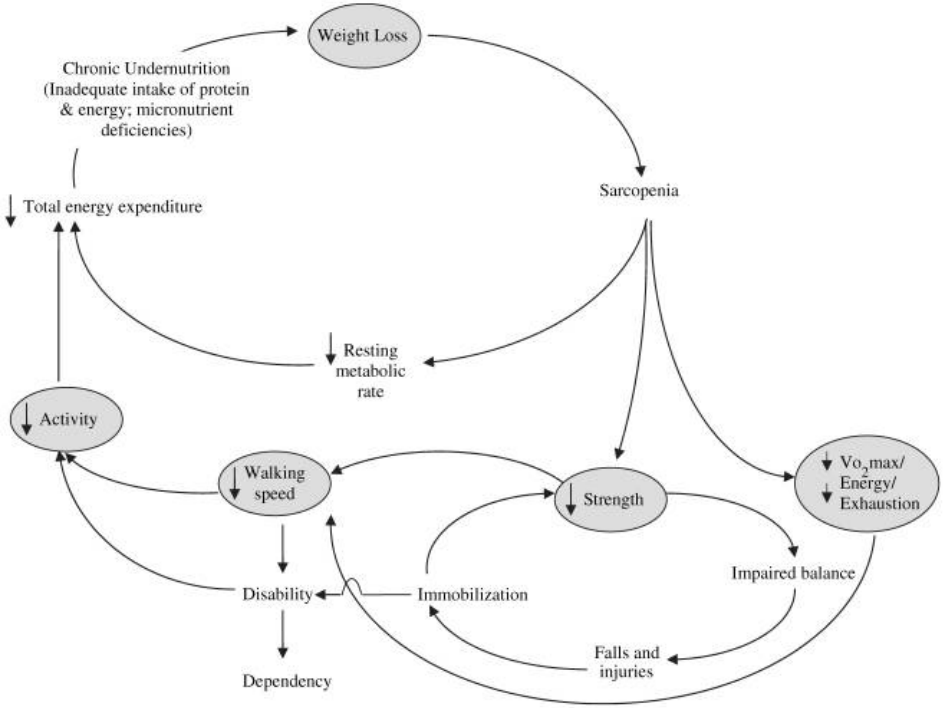
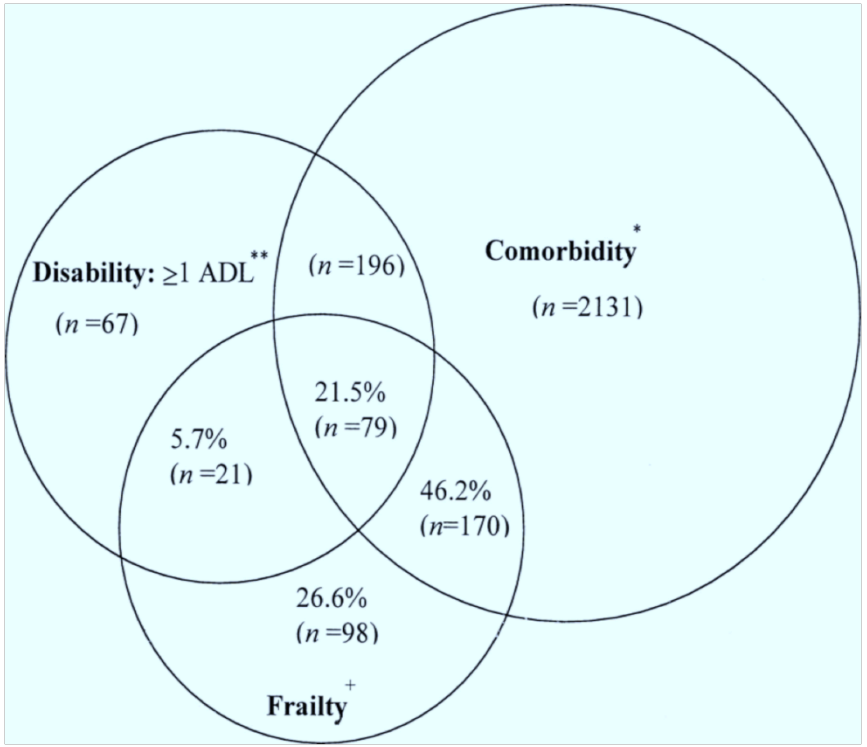
Source: Fried et al, J Gerontol A Biol Sci Med Sci. 2001; 56:M146

Frailty syndrome…



Xue et al, J Gerontol A Biol Sci Med Sci 2008;63(9):984–90



Fried et al, J Gerontol A Biol Sci Med Sci. 2004; 59:255

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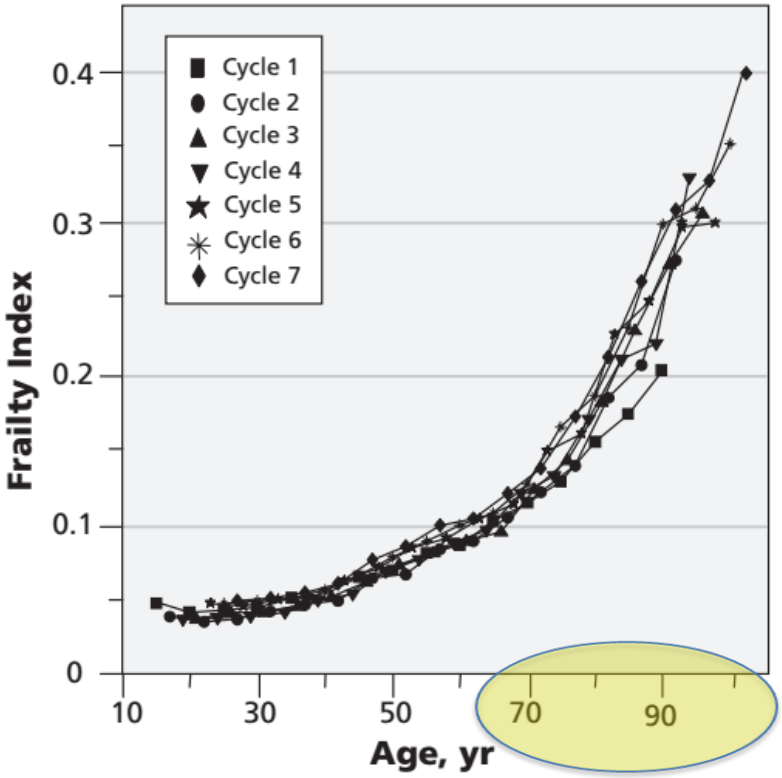
Frailty – Accumulation of Deficits

Frailty Index =

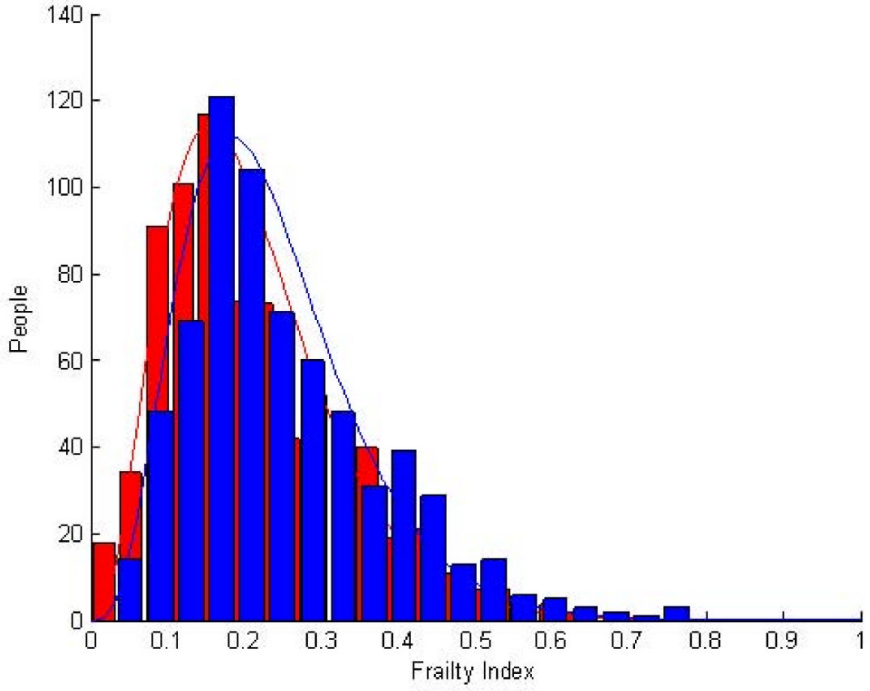
$$\frac{\text{Number of deficits in an individual}}{\text{Total number of deficits measured}}$$

e.g. in a dataset with 40 health deficit measures, a person with 10 things wrong (10 deficits) has a frailty index of 10/40 = 0.25.



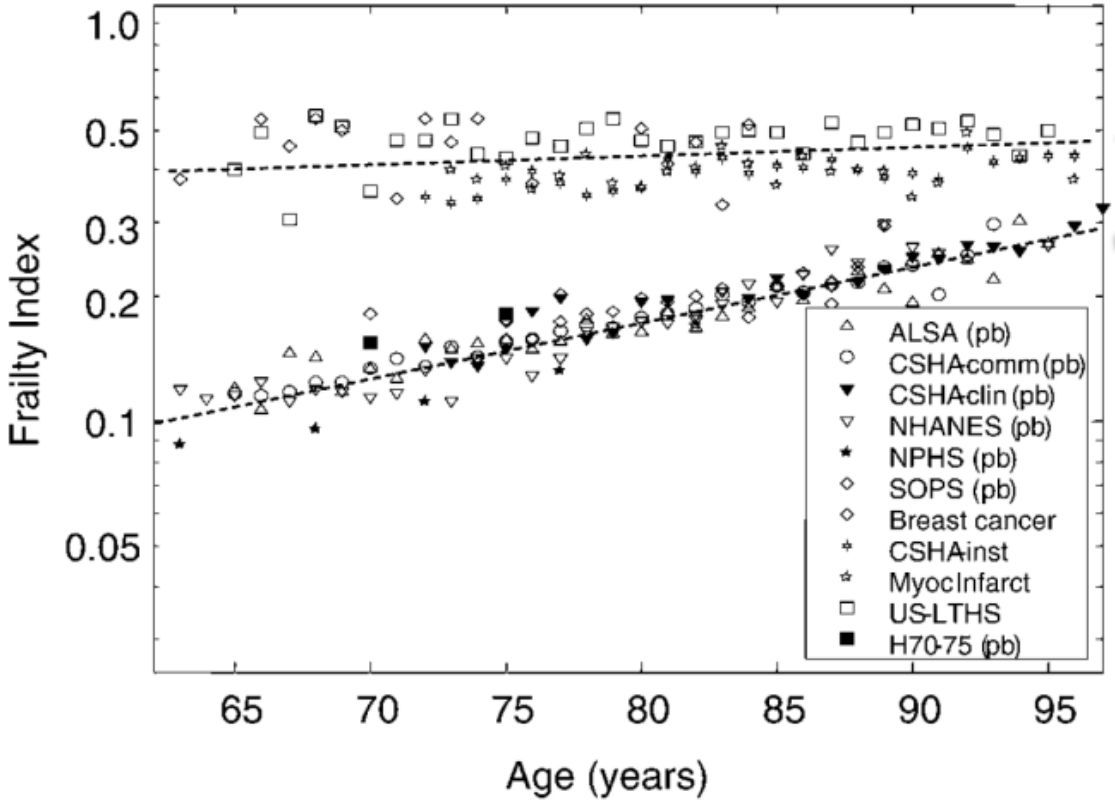
Source: Rockwood et al, CMAJ 2011. DOI:10.1503/cmaj.101271

Frailty: Acquired deficits…



- Mitnitski et al. Accumulation of Deficits as a Proxy Measure of Aging. The Scientific World JOURNAL, 2001;1:323.
- Searle et al. A standard procedure for creating the Frailty Index, BMC Geriatirics, 2008

Frailty: Acquired deficits…



Institutional cohorts

- Population based international cohorts
- Increase 0.03 per year

Rockwood K, J of Gerontology 2007; 62A: 722

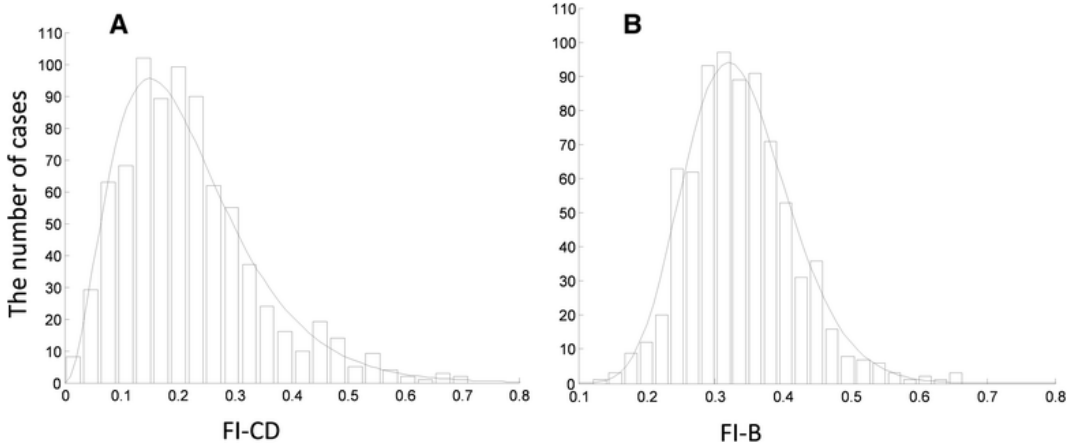
Biology of frailty…

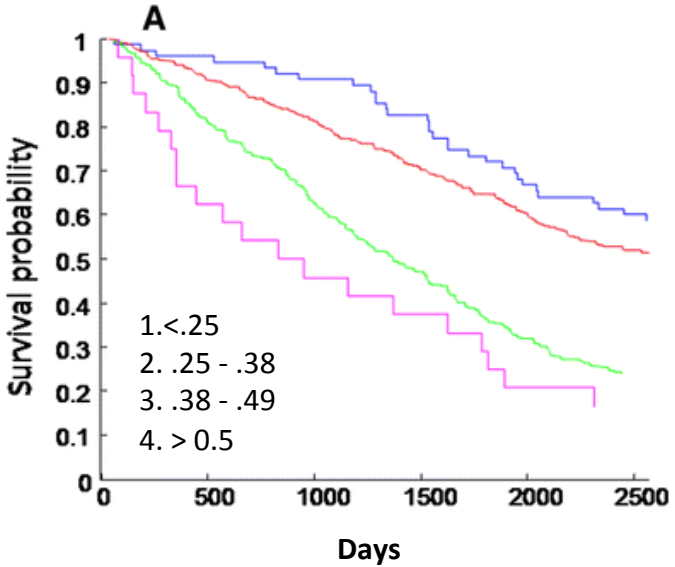
- Frailty not just a clinical construct
- Frailty animal models have been developed
  - Based on chronic inflammation, sarcopenia
- Frailty scales for mice developed
  - Phenotype model: Based on grip strength, walking speed, physical activity, endurance
  - FI based: 31 items deficit model
    - Resveratrol and calorie restriction improved FI

Kane et al. J Gerontol A Biol Sci Med Sci, 2016; 71: 333.

Biology of frailty…

- Human studies point to several mechanisms for frailty including:
  - Oxidative stress, chronic inflammation, immune dysfunction, shortening of telomeres
- FI developed from 40 human biomarkers





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Minitski et al. BMC Medicine 2015; 13: 161.

Biology of frailty…

- FI – LAB:
  - Developed and validated from commonly measured lab values
  - Similar properties to clinical FI
  - Best performance was when clinical and FI-LAB combined
  - Similar performance in Nursing homes

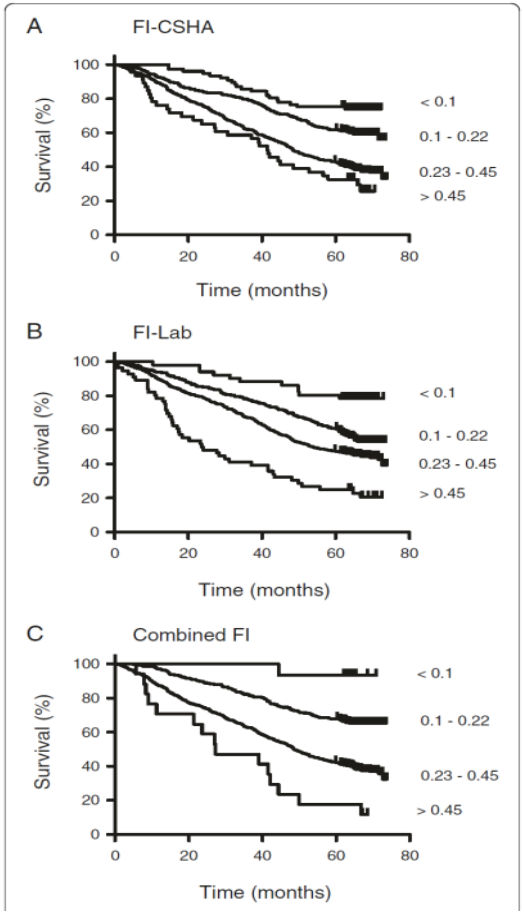


Table 1 Clinical and laboratory data used to construct the FI-LAB

Variable[a]	Low cut-off	High cut-off
Albumin (g/L)	32	45
AST (SGOT; IU/L)	8	33
BP, supine systolic (mmHg)	90	140
BP, supine diastolic (mmHg)	60	90
Calcium (mM)	2.3	2.7
Creatinine (μM)	53	106
Folate (nM)	11	57
Folate, RBC (nM)	376	1450
Glucose, fasting (mM)	3.9	6.1
Hemoglobin (g/L)[b]	135	180
Mean corpuscular volume (fL)	80	96
Phosphatase, alkaline (IU/L)	20	130
Phosphorus, inorganic (mM)	0.74	1.52
Potassium (mM)	3.8	5
Protein, total (g/L)	60	78
Sodium (mM)	136	142
TSH (μIU/L)	0.5	5
Thyroxine (T4; nM)	71	161
T4, Free (pM)	12	30
Urea (mM)	2.9	8.2
VDRL	0	0
Vitamin B12 (pg/L)	118	701
White blood cells (number/L)	1.8×10^9	7.8×10^9

Howlett et al. BMC Medicine 2014; 12: 171.
Rockwood et al, JAMDA, 2015; 16: 842

CLINICAL ASPECTS

Health care system and aging (1)

- **Hospitals**
  - Receive greatest share (37.3%) of public sector health care dollars
    - ICUs account for 10-20% of all hospital costs (up to 40% in the USA)
  - Seniors (> 65 y.o.) account for 40% of acute care stays (14% of population)
  - Seniors (> 65 y.o.) make up 85% of those waiting care elsewhere (ALC)
  - Avg. in-patient RIW in acute care ≈ 70% higher for seniors vs non-senior adults
  - Seniors have higher need of ER services, high rates of hospitalization from ER
  - Seniors' admission to hospital associated with need for long term care and worsening of function including ADL, cognition and continence

Source: Canadian Institute for Health Information, Lakhan, J Am Geri Soc 2011; 59: 2001

Health Care System and Aging (2)

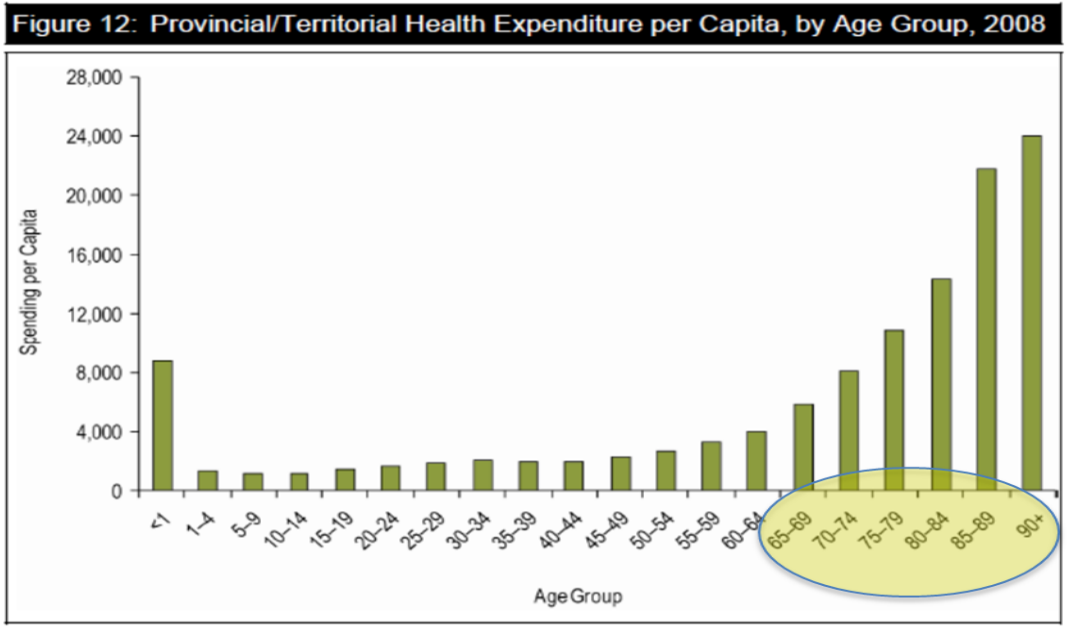
- **Continuing care**
  - Nursing homes/residential care account for ≈ 10% of expenditures
  - In 2009–2010, 95% of people in residential care and 85% of people in hospital-based continuing care were 65+ y.o.
- **Home care**
  - In 2009–2010, 82% of home care clients were 65+ y.o.
- **Prescription drugs**
  - Number of claims rapidly increasing
  - In 2009:
    - 23% of > 65 y.o. and 30% of > 85 y.o. were on 10+ drug classes
    - Governments spent avg. of $1,311/senior vs. $170/adult 20 to 64 y.o.

Source: Canadian Institute for Health Information

Hospitalizations may be preventable

- Earlier detection of deterioration
- Regular monitoring
- Prompt access to a health care provider
- Better medication management
- Better chronic disease management
- Improved support in residence/home

Increasing costs with age

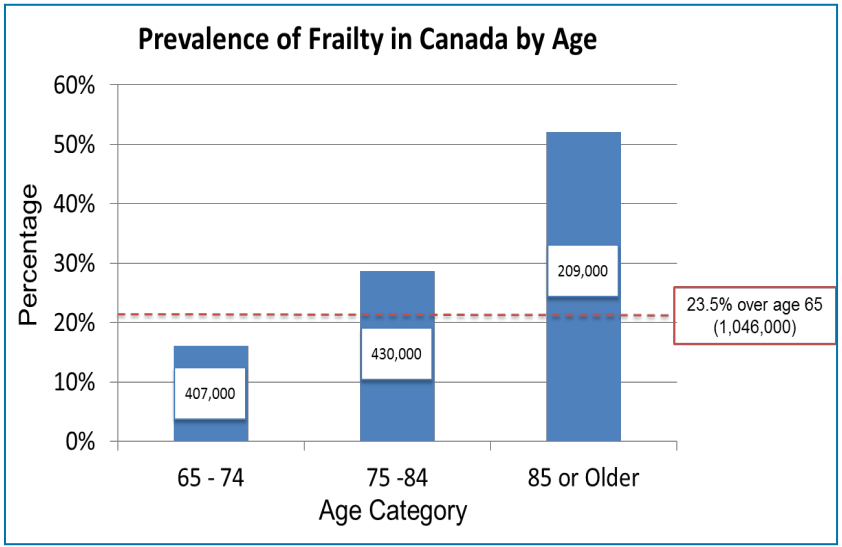


Over 40% of total health care spending occurs in > 65 y.o.; 20% in last year of life

Source: Canadian Institute for Health Information

Frailty in Canadians

- Aging and Frailty are not synonymous but frailty becomes increasingly common as age advances
- Decline in health status and higher health care use driven more by frailty than age



Sources:

1. **Rockwood et al, Journal of Gerontology: 2004; 59: 1310;**
2. **2. statcan.gc.ca/pub/82-003-x/2013009/article/11864-eng.htm**

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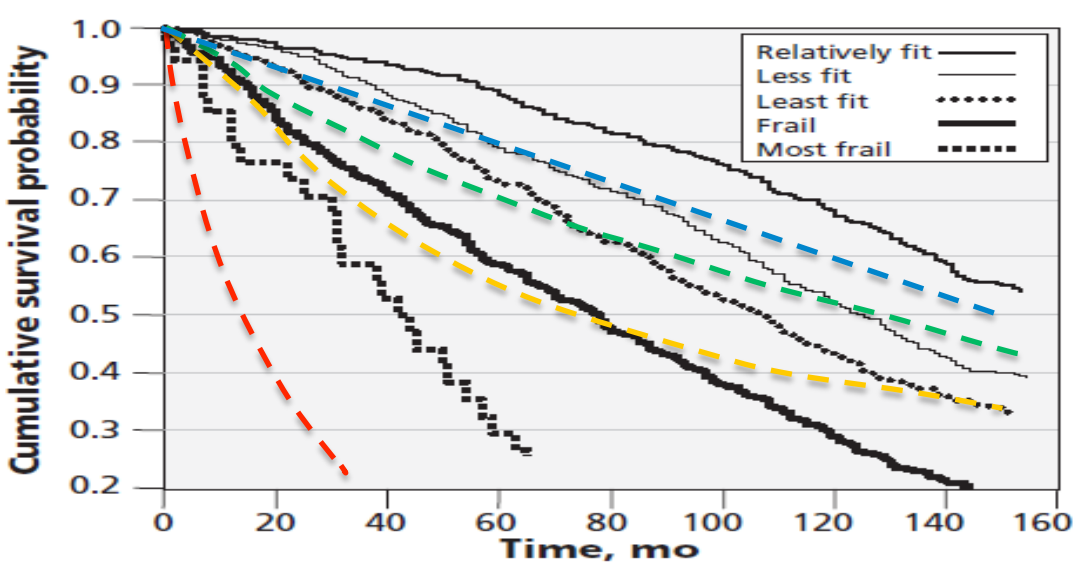
Frailty in The Canadian Health Care System

Patients with frailty over represented in the health care system

- Majority of hospitalized seniors will have pre-frailty or frailty
  - 30 – 40% of ICU patients over the age 50 will have frailty
  - Frailty associated with adverse outcomes and mortality in variety of patient populations
- Majority of seniors in residential care are frail
- Polypharmacy associated with frailty

D Gnjidic, Clin Pharm Ther 2012; 91: 521
Bagshaw, CMAJ doi: 10.1503/cmaj.130639

Correlation of frailty with outcome…community



Colon Cancer
Stage 1
Stage 2
Stage 3
Stage 4

Identification of frailty using the FRAILTY INDEX associated with worsened outcomes, hospitalization and mortality

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Source: Rockwood et al, CMAJ 2011. DOI:10.1503/cmaj.101271

Frailty and hospital discharge…

Table 2: Outcomes within 30 days after discharge, by frailty status

Outcome ≤ 30 d	Frail *n* = 162	Not frail *n* = 333	OR for frailty (95% CI)*		
			Crude	Adjusted for age and sex	Adjusted for age, sex and LACE score†
Readmission or death	39 (24.1)	46 (13.8)	1.98 (1.23–3.18)	2.01 (1.19–3.41)	1.52 (0.87–2.62)
Readmission	36 (22.2)	45 (13.5)	1.82 (1.13–2.97)	1.90 (1.11–3.26)	1.42 (0.81–2.49)
Death	7 (4.3)	6 (1.8)	2.46 (0.81–7.45)	2.18 (0.65–7.39)	1.33 (0.37–4.76)
Visit to emergency department	53 (32.7)	78 (23.4)	1.59 (1.05–2.41)	1.75 (1.10–2.76)	1.43 (0.68–2.30)

Note: CI = confidence interval, OR = odds ratio.
*All models showed nonsignificance on the Hosmer–Lemeshow goodness-of-fit test.
†See Table 1 for explanation of LACE Index.

- Frailty was common among patients
- Frailty was associated with an increased risk of readmission or death within 30 days after discharge .
- Moderate to severe frailty improved the ability to predict rates of readmission or death

Kahlon, CMAJ 2015

Frailty and ICU

- Clinical Frailty Scale
- Worsened outcomes even after adjusting for other indices of severity
- Worsened quality of life post discharge

Bagshaw, CMAJ 2013

Table 3: Clinical outcomes, by frailty status

Outcome	Group; no. (%) of patients*		Association, OR (95% CI) or difference in medians (*p* value†)
	Frail *n* = 138	Not frail *n* = 283	
Adverse event‡	54 (39.1)	83 (29.3)	1.54 (1.01–2.37)
Death			
In ICU	16 (11.6)	27 (9.5)	1.37 (0.72–2.62)
In hospital	44 (31.9)	45 (15.9)	1.81 (1.09–3.01)
Duration of stay, d, median (IQR)			
In ICU	7 (4–13)	6 (3–10)	1 d (0.02)
In hospital	30 (10–64)	18 (10–40)	12 d (0.02)
Discharge disposition§	*n* = 91	*n* = 235	
Home, living independently	20 (22.0)	104 (44.3)	0.35 (0.20–0.61)
Home, living with help	33 (36.3)	58 (24.7)	1.67 (1.00–2.81)
Other¶	38 (41.8)	73 (31.1)	1.51 (0.92–2.48)
Discharged newly dependent**	24 (70.6)	96 (51.6)	2.25 (1.03–4.89)
Hospital readmission§	51 (56.0)	92 (39.1)	1.98 (1.22–3.23)

Note: CI = confidence interval, ICU = intensive care unit, OR = odds ratio.
*Unless stated otherwise.
†Mann–Whitney test.
‡Composite of medication errors, self-extubation/reintubation, nosocomial infection, death.
§Among 91 frail and 235 nonfrail patients for whom data on discharge disposition and on hospital readmission within 12 mo after discharge could be ascertained (data missing, *n* = 1 per group; in hospital at end of follow-up, *n* = 2 per group).
¶Continuing care facility, subacute care facility or other.
**Among 34 frail and 186 nonfrail patients who were living independently at baseline.

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Frailty Index from interRAI AC

- FI-AC derived from 56 potential deficits in interRAI AC
- Increased linearly with age
- Each 0.1 increased the likelihood of inpatient mortality twofold (OR: 2.05 [95% CI 1.70 – 2.48]).

Hubbard, BMC Geriatrics 2015

How can we improve outcomes…

- Minimization or elimination of harm
- Improve outcomes from frailty itself
- Improve healthcare supports or health service delivery for those who are frail

Lack of Evidence

Clinicians, knowledge users and decision makers often face difficult decisions in treating the frail elderly

- Is health care intervention/technology effective in this population?
- Do individual patients/families prefer one kind of technology/ treatment/ care setting over another?
- Is the risk/benefit ratio similar to that of younger or fit patients?
- Is this treatment good value for money?
- Is escalation of acute care interventions warranted?
- When/how should palliative care interventions be instituted?
- What is the most appropriate setting for care?
- How does ACP/EOL care planning fit it?

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The problem

- The frail, the elderly, and those with significant comorbidities routinely excluded from randomized trials
- Similar risks/benefits?
- Applicability or generalizability of evidence?

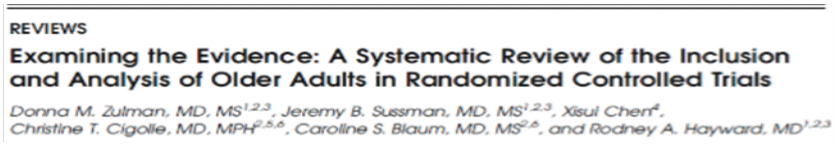
Eligibility Criteria of Randomized Controlled Trials Published in High-Impact General Medical Journals

A Systematic Sampling Review

Harriette G. C. Van Spall, MD
Andrew Toren, MD
Alex Kiss, PhD
Robert A. Fowler, MD, MS

Context Selective eligibility criteria of randomized controlled trials (RCTs) are vital to trial feasibility and internal validity. However, the exclusion of certain patient populations may lead to impaired generalizability of results.

Objective To determine the nature and extent of exclusion criteria among RCTs published in major medical journals and the contribution of exclusion criteria to the rep-



REVIEWS

Examining the Evidence: A Systematic Review of the Inclusion and Analysis of Older Adults in Randomized Controlled Trials

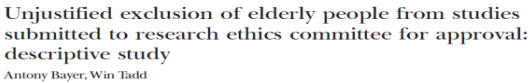
Donna M. Zulman, MD, MS[1,2,3], Jeremy B. Sussman, MD, MS[1,2,3], Xisui Chen[4], Christine T. Cigolle, MD, MPH[2,5,6], Caroline S. Blaum, MD, MS[2,6], and Rodney A. Hayward, MD[1,2,3]

Under-representation of the elderly in clinical trials

H.U. Rehman *

Broomfield Hospital, Broomfield, Chelmsford, Essex, CM1 7ET, United Kingdom

Received 15 July 2005; accepted 4 August 2005



Unjustified exclusion of elderly people from studies submitted to research ethics committee for approval: descriptive study

Antony Bayer, Win Tadd

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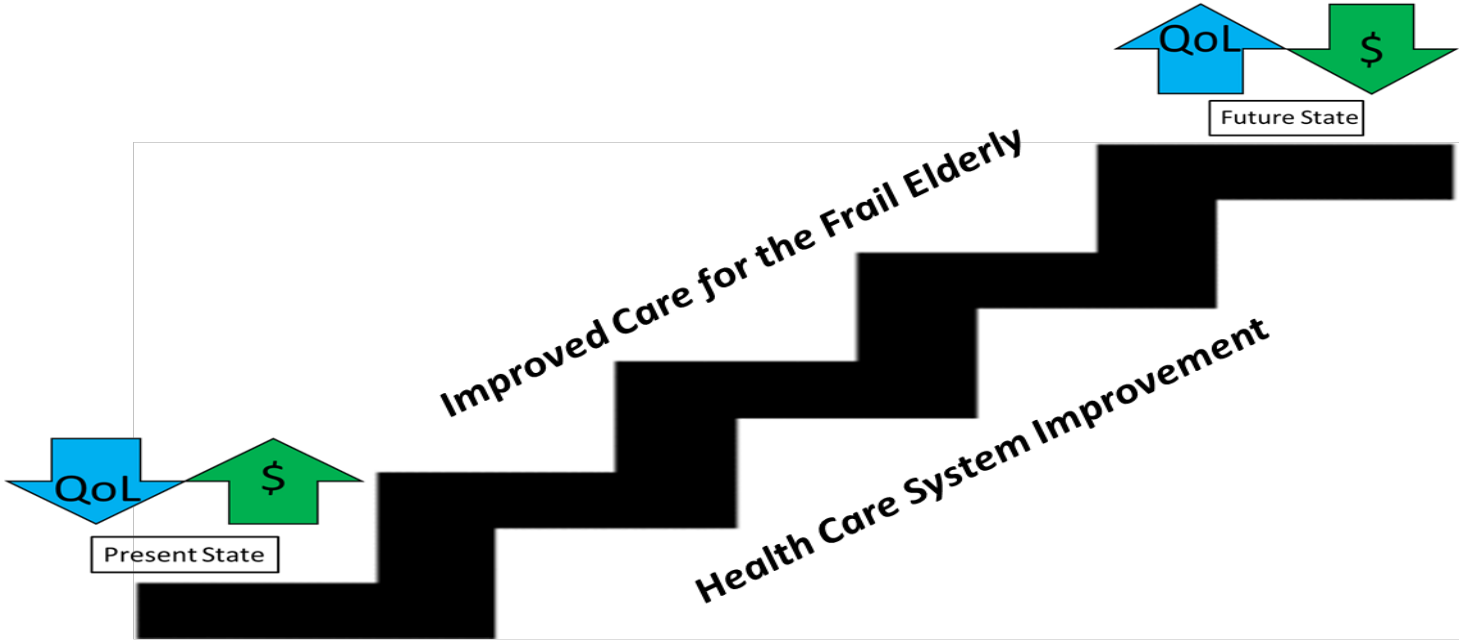
Generalization to the frail elderly…

- Treatments generalized to the frail elderly
  - May not be effective and result in harm or wasted healthcare resources
  - May have been shown to be not effective in non-frail populations but actually be effective in those who are frail

- In the absence of evidence aggressive and expensive technologies are often over used without improvement in outcomes, causing undue suffering and wasted health care resources.

- Escalation may not be wanted

We can do better…



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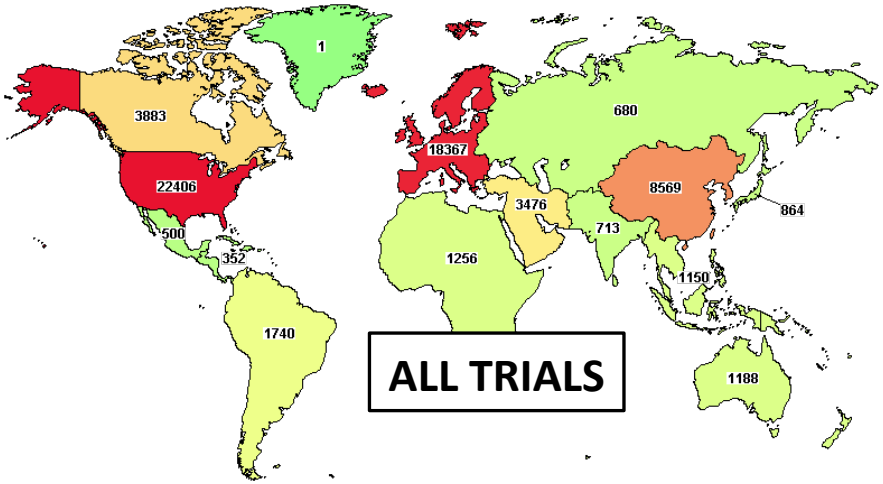
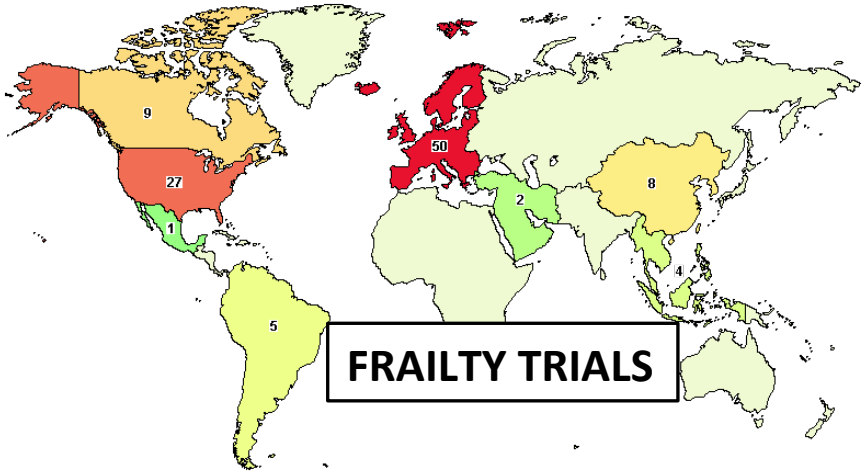
Frailty Trials (clintrials.gov)





61,130 Open Studies

- 46,000 interventional

109 Trials

- 75 Interventional
- 47 Randomized
- 4 interRAI

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Therapeutic interventions for frailty…

Therapeutic Interventions for Frail Elderly Patients: Part I. Published Randomized Trials

Lior Bibas[a,b], Michael Levi[a,b], Melissa Bendayan[c], Louis Mullie[a], Daniel E. Forman[d,e], Jonathan Afilalo[b,c,f,]*

PROGRESS IN CARDIOVASCULAR DISEASES 57 (2014) 134–143

- 38 RCTs reported
- Most were small (1 > 1000 pts)
- Outcomes varied:
  - Change in frailty scale, mobility, strength, weight, gait speed, insulin resistance, muscle mass

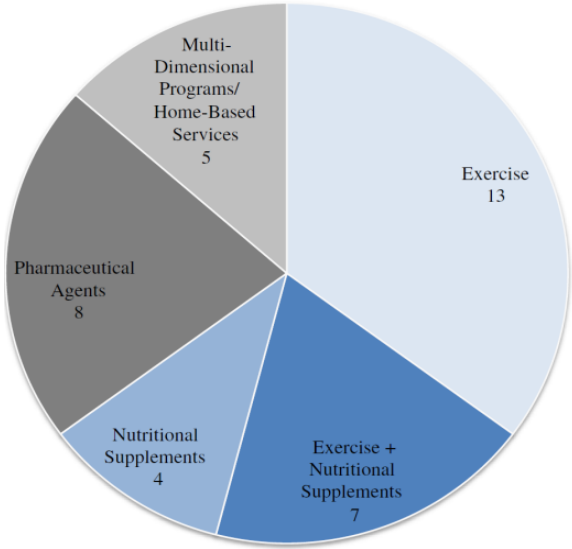

Fig 2 – Interventions studied.

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Therapeutic interventions for frailty…

BMJ Open

Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a protocol for a scoping review of the literature and international policies

Martine T E Puts,[1] Samar Toubasi,[1] Esther Atkinson,[2] Ana Patricia Ayala,[3] Melissa Andrew,[4] Maureen C Ashe,[5] Howard Bergman,[6] Jenny Ploeg,[7] Katherine S McGilton[1,8]

Clinical aspects - conclusion

- Frailty associated with worsened outcomes
- Little evidence to guide care
- High need for more interventional trials
    - System organization/health care supports
    - Interventions for frailty
    - Reduction of adverse events
    - Better EOL care/ACP

What is the right outcome…

- Measures of Frailty
- Patient centered outcomes
  - Morbidity, Mortality, QOL Measures
- Health system Outcomes
  - Utilization, health resource consumption

What is the right outcome… frailty measures

Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

Outcome instruments to measure frailty: A systematic review

N.M. de Vries[a,*], J.B. Staal[a], C.D. van Ravensberg[b], J.S.M. Hobbelen[c,d],

- 20 potential instruments
- Conclusion:
  - Frailty index the most promising
    - *Continuous scoring system*
    - *Influence of non-changeable items in index*
    - *Clinometric properties need to be studied further*

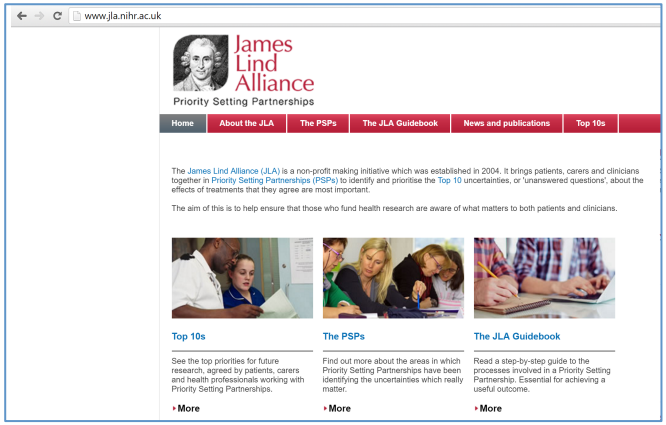
What is the right outcome…

- Survey of elderly citizens ranking potential outcomes for critical studies
  - Highest ranking or most important
    - Permanent neurological dysfunction
    - Quality of Life
    - Long term disability requiring institutional care
  - Lowest ranking or least important outcomes
    - Duration of hospitalization
    - Mortality
    - Delirium

Muscedere et al, ESICM 2015

Citizen engagement in research…

- Guide research priorities
  - James Lind Process
- Conduct of Research
  - Steering committees,
  - Interpretation of results, communication
- Implementation
  - Outreach to the public



Frailty screening

- Early identification of frailty with the institution of appropriate care plans is paramount.
- Frailty screening:
  - Mass screening (wholescale screening of large populations) to case finding or opportunistic screening (screening of populations who consult health services for another purpose).
  - Case finding can systematically or opportunistically identify individuals from a larger population for a specific purpose (e.g. comprehensive geriatric assessment).
  - Although mass screening has been advocated by some organizations, it remains controversial;
    - British Geriatrics Society advocate for case finding or opportunistic screening.

Development and validation of an electronic frailty index using routine primary care electronic health record data

Andrew Clegg[1*], Chris Bates[2], John Young[1], Ronan Ryan[3], Linda Nichols[3], Elizabeth Ann Teale[1], Mohammed A. Mohammed[4], John Parry[5], Tom Marshall[3]

Age and Ageing 2016; **0:** 1–8
doi: 10.1093/ageing/afw039

Results: we include data from a total of 931,541 patients. The eFI incorporates 36 deficits constructed using 2,171 CTV3 codes. One-year adjusted HR for mortality was 1.92 (95% CI 1.81–2.04) for mild frailty, 3.10 (95% CI 2.91–3.31) for moderate frailty and 4.52 (95% CI 4.16–4.91) for severe frailty. Corresponding estimates for hospitalisation were 1.93 (95% CI 1.86–2.01), 3.04 (95% CI 2.90–3.19) and 4.73 (95% CI 4.43–5.06) and for nursing home admission were 1.89 (95% CI 1.63–2.15), 3.19 (95% CI 2.73–3.73) and 4.76 (95% CI 3.92–5.77), with good to moderate discrimination but low calibration estimates.

Conclusions: the eFI uses routine data to identify older people with mild, moderate and severe frailty, with robust predictive validity for outcomes of mortality, hospitalisation and nursing home admission. Routine implementation of the eFI could enable delivery of evidence-based interventions to improve outcomes for this vulnerable group.

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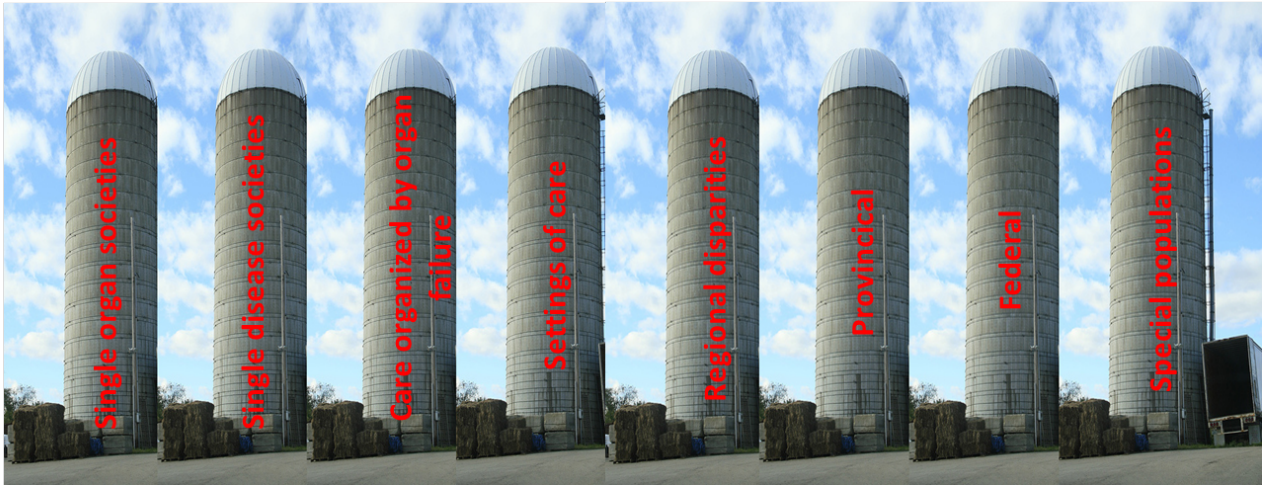
Conclusion…



To address frailty in the Canadian Health Care system, we need a multi-pronged approach including increasing its recognition, increasing the evidence for its treatment and multi-institution, multi-jurisdictional efforts including breaking down silos in the system

Questions?