Addressing frailty in healthcare systems including critical care.

Is a network the answer?

Dr. John Muscedere,
Professor of Medicine, Queen’s University
Scientific Director, Canadian Frailty Network (CFN)
Dr. John Muscedere

- Scientific Director and CEO for the Canadian Frailty Network which is funded by the Government of Canada through the Networks of Centers of Excellence (NCE).
  - CFN partners with governmental entities, NGOs and commercial entities including pharmaceutical corporations

- Relationship with commercial interests:
  - Consulting: PolyPhor Pharma
Outline

• Aging and healthcare systems
• Frailty and its impact
• Path Forward
Aging - Global Perspective

Sources: United Nations:
World Population Prospects: The 2010 Revision
Aging in Canada

- Proportion over the age of 65 is increasing
- Older (over age 85) growing rapidly
- Present: 4.46 working adults for every 1 senior
- Future: < 3 working adults for every 1 senior (by late 2020s)

Source: Health Care in Canada, 2011: A Focus on Seniors and Aging, CIHI
Disability with age

Source: Canadian Institute for Health Information
Shift in the Aging Curve

Not all aging is the same. How do we risk stratify?

Healthy Aging

Frailty

Multi-morbidity, Loss of functional capacity
The Frailty: Definition

• 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.

• ‘Minor’ events trigger major changes in health status

• Increased risk of physical, cognitive and functional decline, adverse health outcomes and mortality

Source:
How is Frailty measured?

• Pathophysiology of frailty includes loss of function in the neuromuscular, neuroendocrine and immunological systems
  – Increased risk of inability to maintain homeostasis

• Validated scales available (deficit model or phenotype model)
  – No consensus

• Frailty described in critically ill: Clinical Frailty Scale, Frailty Index, Frailty phenotype

Viña et al, 2016, Molecular Aspects of Medicine 50; 88–108
Frailty in Canadians

Fig. 1 Prevalence of frailty across age categories and frailty definition

Prevalence of Frailty in Canada by Age (> 65 y.o.)

Sources:
1. statcan.gc.ca/pub/82-003-x/2013009/article/11864-eng.htm
2. Kehler et al, BMC Geriatrics 2017

23.5% over age 65 (1,046,000)
Health Care System and Frailty (1)

Hospitals

- Receive 37% of public sector health care dollars
  - ICUs: 10-20% of all hospital costs
- Seniors (> 65 y.o.) account for 40% of acute care stays (14% of population)
  - Over 50% of ICU patients are seniors
- In-patient RIW ~70% higher for seniors vs non-senior adults
- Hospitalization in seniors associated with need for long term care and worsening of function including ADL, cognition and continence
- Majority of hospitalized seniors are of frail
- Frailty associated with adverse outcomes and mortality in variety of patient populations and acute care interventions

Source: Canadian Institute for Health Information
Health Care System and Frailty (2)

Hospitals and Alternative Level of Care (ALC)

• It is estimated that at any one time there are 7500 hospital beds occupied by seniors waiting to receive care in another setting
  - Represents 14% of hospital beds
  - ALC estimated to cost $2.5 Billion per year
• Seniors make up 85% of those waiting care elsewhere
  - > One third over the age of 85
  - > One quarter have dementia
• Presence of frailty predicts risk of ALC and likely that majority of ALC are frail

Source: Canadian Institute for Health Information
Sutherland, Healthcare Policy 2013
Health Care System and Frailty (3)

Continuing Care – Long-term Care

- Over 350,000 live in long term care homes
  - People enter LTC homes later in their life course with multiple medical conditions
  - Almost half of LTC residents are over the age of 85
  - Public costs of LTC account for ≈ 10% of healthcare expenditures
  - Total costs of LTC in 2014 was ~$69 billion- increase to $188 billion by 2050.
- Almost all residents of LTC are frail

Home Care

- 2.2 Million Canadians received home care in 2012
- Frailty present in 20 – 40% depending on measurement used

Canadian Institute for Health Information
CD Howe Institute; 2014
Statistics Canada; 2014, 2015
Campitelli et al, BMC Geriatrics 2016
What do we know about frailty in ICU – Systematic Review and Meta-analysis

• 10 observational, prospective studies comparing outcomes between frail and non-frail patients as identified on admission
• 3030 patients enrolled: 927 Frail
• 7 Used CFS, 4 FI and 2 FP
• Age criteria varied: >18, > 55, > 65 > 80 y.o.

Muscenede et al, Intensive Care Medicine 2017
Frailty in ICU: Prevalence

Study                Prev (95% CI)
Bagshaw 2014         0.32 (0.28, 0.37)
Brummel 2016         0.30 (0.27, 0.32)
Fisher 2015          0.14 (0.09, 0.19)
Heyland 2015         0.32 (0.28, 0.35)
Hope 2015            0.35 (0.25, 0.45)
Hope 2017            0.35 (0.26, 0.45)
Kizilarslanoglu 2016 0.21 (0.14, 0.29)
Maguet 2014          0.23 (0.18, 0.30)
Mueller 2015         0.37 (0.28, 0.47)
Zeng 2015            0.60 (0.52, 0.68)

Overall              0.30 (0.29, 0.32)
I² = 91%
Impact of frailty on mortality

a. Hospital Mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Frail Patients</th>
<th>Non-frail Patients</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bagshaw 2014</td>
<td>44</td>
<td>138</td>
<td>45</td>
<td>283</td>
<td>15.4%</td>
<td>2.01 [1.40, 2.88]</td>
</tr>
<tr>
<td>Brummel 2016</td>
<td>84</td>
<td>307</td>
<td>130</td>
<td>733</td>
<td>23.5%</td>
<td>1.54 [1.21, 1.96]</td>
</tr>
<tr>
<td>Fisher 2015</td>
<td>3</td>
<td>28</td>
<td>23</td>
<td>177</td>
<td>2.4%</td>
<td>0.82 [0.26, 2.57]</td>
</tr>
<tr>
<td>Heyland 2015</td>
<td>63</td>
<td>193</td>
<td>95</td>
<td>416</td>
<td>21.2%</td>
<td>1.43 [1.09, 1.87]</td>
</tr>
<tr>
<td>Hope 2015</td>
<td>11</td>
<td>29</td>
<td>6</td>
<td>55</td>
<td>3.8%</td>
<td>3.48 [1.43, 8.44]</td>
</tr>
<tr>
<td>Hope 2017</td>
<td>11</td>
<td>34</td>
<td>6</td>
<td>61</td>
<td>3.7%</td>
<td>3.29 [1.33, 8.11]</td>
</tr>
<tr>
<td>Kızıllarslanoğlu 2016</td>
<td>19</td>
<td>26</td>
<td>27</td>
<td>59</td>
<td>15.4%</td>
<td>1.80 [1.11, 2.30]</td>
</tr>
<tr>
<td>Maguet 2014</td>
<td>23</td>
<td>46</td>
<td>42</td>
<td>150</td>
<td>14.2%</td>
<td>1.72 [1.21, 2.63]</td>
</tr>
<tr>
<td>Mueller 2015</td>
<td>5</td>
<td>39</td>
<td>0</td>
<td>63</td>
<td>0.4%</td>
<td>17.60 [1.00, 309.78]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>840</strong></td>
<td><strong>1997</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>1.71 [1.43, 2.05]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 263 374
Heterogeneity: \(\tau^2 = 0.02\); \(\chi^2 = 11.76\), df = 8 (\(P = 0.16\)); \(I^2 = 32\%\)
Test for overall effect: \(Z = 5.79\) (\(P < 0.00001\))

b. Long-term Mortality (≥ 6 Months)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Frail Patients</th>
<th>Non-frail Patients</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
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<td>60</td>
<td>283</td>
<td>8.0%</td>
<td>1.54 [1.11, 2.14]</td>
</tr>
<tr>
<td>Brummel 2016</td>
<td>158</td>
<td>307</td>
<td>251</td>
<td>733</td>
<td>39.5%</td>
<td>1.50 [1.30, 1.74]</td>
</tr>
<tr>
<td>Heyland 2015</td>
<td>106</td>
<td>193</td>
<td>146</td>
<td>417</td>
<td>25.8%</td>
<td>1.57 [1.31, 1.88]</td>
</tr>
<tr>
<td>Hope 2017</td>
<td>15</td>
<td>34</td>
<td>16</td>
<td>61</td>
<td>2.7%</td>
<td>1.68 [0.96, 2.96]</td>
</tr>
<tr>
<td>Kızıllarslanoğlu 2016</td>
<td>22</td>
<td>26</td>
<td>59</td>
<td>96</td>
<td>16.6%</td>
<td>1.38 [1.10, 1.73]</td>
</tr>
<tr>
<td>Maguet 2014</td>
<td>27</td>
<td>46</td>
<td>45</td>
<td>150</td>
<td>7.3%</td>
<td>1.96 [1.39, 2.76]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>744</strong></td>
<td><strong>1740</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>1.53 [1.40, 1.68]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 373 577
Heterogeneity: \(\tau^2 = 0.00\); \(\chi^2 = 3.06\), df = 5 (\(P = 0.69\)); \(I^2 = 0\%\)
Test for overall effect: \(Z = 9.02\) (\(P < 0.00001\))
Other outcomes...

- No difference in Hospital, ICU LOS, utilization of MV (approx. 80%), Vasoactive therapy (approx. 56%)

- Discharge home: frail patients much less likely be discharged home (RR 0.59, 95 CI, 0.49, 0.71; p < 0.00001, I² = 12%)

- QoL- worse in frail patients (2 studies)

- Increasing frailty correlated with worsened outcomes

- Nine studies reported adjusted outcomes.
  - Worsened outcomes for frail patients in spite of adjusting for age, illness severity, co-morbidities
  - Pooled adjusted mortality: 3 studies, 1657 pts
    RR 1.75 (1.36, 2.24), p < 0.0001, I² = 43%
The Problem – Lack of Evidence (1)

Care providers and decision makers often face difficult decisions when treating the frail elderly but high quality evidence for decision making is often lacking.

Evidence is lacking because:

- The frail/those with significant comorbidities are often excluded from trials
- Trials enrolling older adults rarely consider differential impact of frailty
- Few frailty clinical trials

Questions:

- Similar risks/benefits?
- Applicability or generalizability of evidence?
The Problem – Lack of Evidence (2)

Because of the lack of evidence:

• Treatments that are effective in fit patients are often applied to those with frailty
  ➢ May not be effective and result in harm or wasted resources
  ➢ Expensive technologies are often aggressively used on frail patients without improvement in outcomes especially in the ICU

• Treatments not effective in fit patients may actually be effective in those who are frail
Frailty Publications Per Year

Source: PubMed
Therapeutic interventions for frailty

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

Scoping review of community based interventions

• 14 Studies were found (12 RCTs, 2 cohort studies)
• Intervention in 9 Studies reduced level of frailty
• Variety of interventions including physical activity (4), physical activity + nutrition (4), physical activity + nutrition + memory training, home modifications (1), physical therapy + exercise + home modifications (1), geriatric assessment (3)
• Variety of frailty definitions and outcomes

Source: Puts et al, Age and Ageing, 2017
Frailty Trials (clintrials.gov)

241,362 Registered Studies
- 193,369 (80%) interventional
- 129,486 (54%) Randomized

352 Registered Studies
- 270 (76%) Interventional
- 181 (51%) Randomized
Problem with use of current evidence for decision making

1. Studies to date have used a variety of population descriptors, frailty measurements or no objective measures of frailty
2. Outcomes reported vary with many not being patient centered or health system outcomes
3. Limited interpretability, comparability and aggregation possibilities for studies
4. Reduced ability for valid study to study comparisons or generalizability/applicability.
5. No studies of differential impact of frailty on interventional outcome
6. No interventional studies of frailty in critically ill
Knowledge Gaps for Frailty and Critical Care

• Identification of Frailty
  – When to measure/determine frailty
  – How to best measure/assess frailty

• What is the interaction between frailty and critical illness?
  – How does critical illness modify the course of frailty?
  – How does frailty impact the course of critical illness?

• How do we improve outcomes of critically ill frail patients? Frailty may modify impact of interventions/processes of care:
  – Intervention effective in fit patients lack effect or cause harm in frail pts
  – Intervention not effective in fit patients may be effective in frail patients
  – No ICU interventional study has studied the impact of frailty on the efficacy of the intervention proposed
Network Utility

1. Bring a community of researchers together
   • Multidisciplinary research
   • Promote research across settings of care
   • Provision of seed funding

2. Increase quantity and quality of frailty research
   • Promotion of increased number of interventional trials
   • Standardized core data elements in frailty studies
   • Standardized common outcomes in frailty studies

3. Move towards open data in frailty studies

4. Knowledge Mobilization by bringing together decision makers, stakeholders, patients to increase adoption of evidence
Activity in CFN’s first term ending July 2017

- **Investment in 88 research projects during our first term**
- **121** Principal Investigators, **421** Co-investigators
- $19.7 Mil. total research funding ($12.8 Mil. from CFN + $6.9 Mil. partner contributions)
- $10 Mil from other research agencies
- **57** Interventional studies
- **Prior to CFN:** only 93 frailty papers reported from Canada – only 22 studied an intervention

*Numbers add up to greater than 88 since some grants covered more than one theme*
Conclusion

• Frailty will become increasingly prevalent in our society from an aging population but also due to our ability to improve survival

• Frailty will increasingly challenge our healthcare system

• The multi-dimensional nature of frailty will require coordinated effort across the healthcare system

• Investigation of frailty in critical care in its infancy

• Networks composed of researchers, stakeholders, decision-makers, patients and caregivers are the only way that the complex problems posed by frailty can be addressed
Questions?
Prescription drugs

- Number of claims rapidly increasing
- In 2012:
  - nearly 2/3 of seniors (65 and older) take 5 or more drugs
  - 39.3% > age 85 claims for 10 or more drug classes
  - ½ of seniors living in LTC facilities are on 10 or more different drug classes
- Polypharmacy associated with frailty
- Frailty and polypharmacy associated with adverse outcomes
- Frailty is a predictor of inappropriate prescribing and Adverse Drug Reactions

Canadian Institute For Health Information, 2012
Cullinan et al, Age and Ageing, 2016
Saum et al, J Am Geriatrics Soc, 2017
Rosted et al, Dan Med J, 2016
Barriers to be addressed to improve frailty care

1. Frailty is under-recognized and its impact is under-appreciated
2. The healthcare system is organized around single disease, single organ dysfunction
3. Fragmentation of the healthcare system
4. There is little high quality evidence available to guide care for frailty