Review of e-Frailty Evaluation Frameworks

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This paper outlines some of the key methods used to evaluate frailty and provide important metrics for the implementation of an e-Frailty framework. Frailty is an emergent property of the aging process, as measured using quantification of accumulation of deficits (Frailty Index) or as observed functional impairment (Phenotype Model)

Frailty, e-Health Framework, patient records

1. INTRODUCTION

Frailty as defined by P. Moorhouse et al in the journal of the Royal College of Physicians of Edinburgh as "…a progressive physiological decline in multiple organ systems marked by loss of function, loss of physiological reserve and increased vulnerability to disease and death."[12] Additionally and more commonly stated as an "accumulation of deficit "[11].

There has been historically little consensus [5] on what a clinical definition of frailty actually is because it does not present as a syndrome in which symptoms are easily visualised [6]. However, in general terms clinicians use experience and guidelines such as that from the I.A.N.A Task Force that describes frailty as "…a commonly used term indicating older persons at increased risk for adverse outcomes such as onset of disability, morbidity, institutionalisation or mortality or who experience a failure to integrate adequate responses in the face of stress."[7]

However, as Kenneth Rockwood et al., demonstrates, frailty can be calculated mathematically from a population at any age [8], so frailty is not just the preserve of the old. Although, is it true to say that most of the clinically frail are greater that 50 years of age [9]. In fact, it is estimated that 7% of individuals greater than 65 years of age are affected [10].

To provide a starting point and understand the complex shift in the evolving demographics of the United Kingdom, it is useful to look at the projected life expectancy of the UK population. From Figure 1, it is clear to see that the actual years lived (pre 2012) and the projected life expectancy (post 2012) have a significant increase to the year on year life expectancy and females on average living approximately 5 to 7 years longer than a male. However, the ONS (2014) stated that over a 40-year period (1971-2011) there was a 2.0% for male and 1.5% for female improvement in the average annualised aggregated standardised mortality rate. This indicates that at some point in the future (if all things remain equal) the 5 to 7 year life expectancy difference between male and female life expectancy will be eroded away due to the 0.5% differential in improvement.

The take away information from the ONS is that inequality of life expectancy between the sexes is being eroded year on year, and that men and women are living longer than at any other time in history.

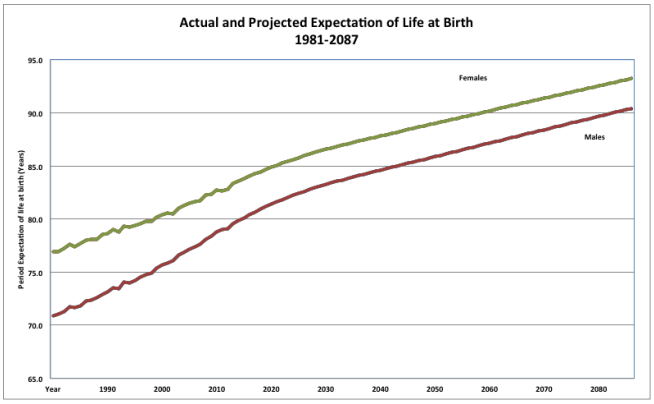


Figure 1 – ONS Actual and Projected Period Life 1981-2087 [2]

The National Records for Scotland (NRS) included within their submission to the Scottish Parliament Finance Committee on demographic change and an aging population, that the 2011 census day estimates indicated that the population had increased at the fastest rate between two census years, which represented a 5% growth of 233,000 on a population of 5,295,000 and that more importantly the size of the population over 65 has grown from 5% to 17%.

Understanding that the demographic change is implicit and cannot be materially affected in any significant or short-term way, results in the conclusion that the issue at hand becomes one of

management. As the data outlines, Scotland has greater need than England, and although the Scottish population is growing generally, the aging population of 65 years old and over, is growing at a significantly faster rate than the underlying population growth.

The weight of compelling evidence suggesting the significance in the potential adverse change in population demographics prompted the Scottish Government Chief Scientist Office to fund a study by Barnett et al. (2012) within Scotland to look at and determine the '*Epidemiology of multi-morbidity and implications for health care, research and, medical education*'[13].

The significance of the study, was that Barnett et al. (2012) were able to provide evidence that challenged the '*single-disease framework*' doctrine which is embedded within current health care, medical research and medical education. It was then suggested that a complementary strategy was required, that would support GP's and generalist clinicians to provide '*comprehensive and personalised continuity of care in socioeconomically deprived areas'*.

Fundamentally, it is not too much of a leap to conclude that '*an accumulation of deficits*' and '*multi-morbidity*' are physically at least, so similar as to be the same for most purposes. The research unfortunately from Barnett et al. (2012) did not directly gather any socioeconomic or deprived community information and the data was taken from a database (March 2007) that was a number of years older than that of the study.

This realisation of the fundamental '*single-disease framework*' problem that exists within the health-care system, combined with that of identifying that a patient has multi-system health degradation, then only treating one of the underlying conditions at a time, usually in isolation, (as the clinicians are specialists) provides a clear opportunity for improvement.

2. MULTIMORBIDITY

Mitniski, Mogilner & Rockwood (2001)[i] proposed 'An accumulation of Deficits' as a proxy measure of aging, which has been a widely accepted definition and investigated further[1]. As the research from Barnett et al. (2012)[2] Figure 2 highlights, multi-morbidity significantly increases with age. Another significant influence on multi-morbidity is that of social status. Figure 3 highlights research from Barnett et al. (2012). Research showed that multi-morbidity increased with local deprivation in which the patient lived.

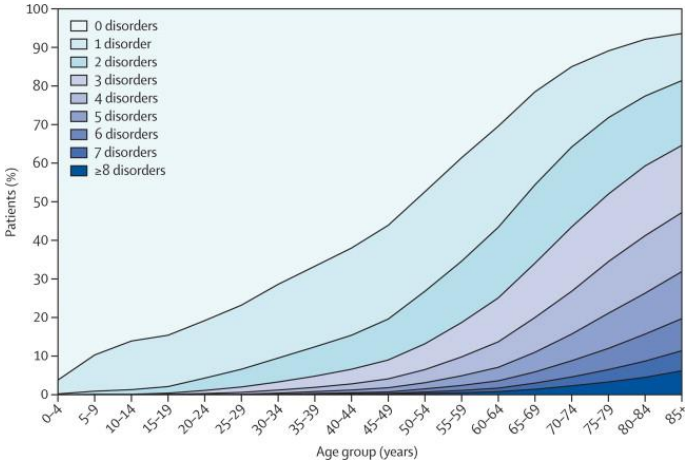


Figure 2 - Number of Chronic disorders by age group

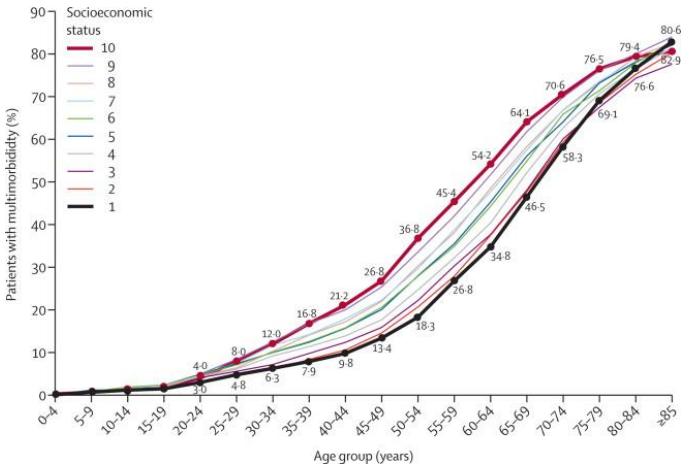


Figure 3 - Prevalence of multimorbidity by age and socioeconomic status

3. FRAILTY

Frailty is a complex and multifaceted issue that has been evolving dramatically over the last 30 years[ii]. The two most often used approaches to characterize frailty are to operationalize frailty via a phenotype model [12,13,14] based on observed or reported physical characteristics or an index model[15,16,17] based on the quantification of accumulated deficit.

Leocadio Rodríguez-Maňas et al. [18] outlines the lack of agreement regarding the definition of frailty for clinical uses, and uses a modified Delphi process to achieve expert consensus for frailty. The results outlined that only 44% overall of the statements regarding the concept of frailty and 18% of the statements regarding diagnostic criteria were accepted. There was agreement on the value of screening for frailty and on the identification of six domains of frailty for inclusion in a clinical definition; however, no agreement was established for laboratory biomarkers useful for diagnosis.

However, Fischer et al. (2014) was able to establish biomarkers for the '*Predication of all-cause Mortality*'[19] by Nuclear Magnetic

Resonance Spectroscopy (NMR). The study took 106 candidate biomarkers from blood plasma in an Estonian Biobank and found that four circulating biomarkers predicted all-cause mortality:

- ***Alpha-1-acid glycoprotein*** (hazard ratio [HR] 1.67 per 1–standard deviation increment, 95% CI 1.53–1.82, p=5610231)
- ***Albumin*** (HR 0.70, 95% CI 0.65– 0.76, p=2610218)
- ***Very-low-density lipoprotein particle size*** (HR 0.69, 95% CI 0.62–0.77, p=3610212), and
- ***Citrate*** (HR 1.33, 95% CI 1.21–1.45, p=5610210).

The four biomarkers were predictive of the risk of short-term death from cancer, cardiovascular mortality in addition to nonvascular diseases, and in fact 20% of those from the Estonian Biobank cohort that scored within the highest percentile died within the first 12 months of the follow-up, which indicated significant systemic frailty-like activity. The Estonian study was replicated and validated by a Finnish cohort.

Rodríguez-Mañas et al. (2013) determines that the considered domains (and criteria) of frailty which should be validated in cultural, economic, ethnic and clinical settings[20] such that they demonstrate their predictive validity for adverse outcomes[21,22] are:

- Nutritional Status (Weight Loss)
- Energy (Exhaustion)
- Physical Activity (Leisure time activity)
- Mobility (Gait speed)
- Strength (Grip Strength)
- Cognition
- Mood
- Mental Health [23,24]

The phenotype of frailty includes: Sarcopenia; Cachexia; Anorexia; Osteoporosis; Fatigue; Risk of falls; and Poor physical health.

EARLY WARNING AND PREVENTION

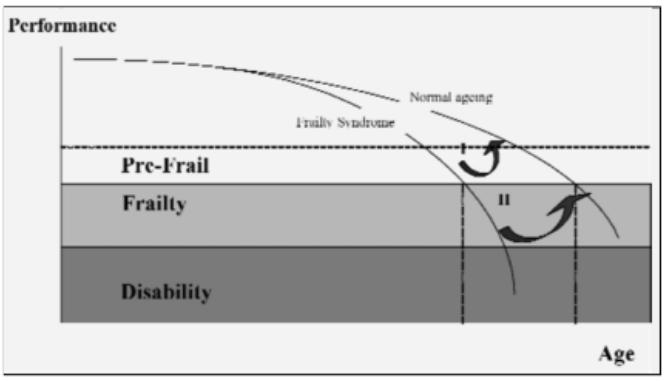
Mohandas states that earlier research suggests that customised interventions may reverse some of the physical consequences of frailty [25]. A randomised trial with two groups of elderly people that were 75 years or older was carried out by Andreas Stuck et al [26]. The *"Intervention"* group consisted of 215 people and were seen at home by gerontologic nurse practitioners who, in collaboration with geriatricians, evaluated problems and risk factors for disability, gave specific recommendations, and provided health education. The second *"control"* group consisted of 199 people that only received their regular medical care. The results at three years were that 12% of the intervention group and 22% of the control group required basic assistance in performing the basic activities (bathing, dressing, feeding, grooming, transferring from bed to chair, and moving around inside the house) of daily living (adjusted odds ratio, 0.4; 95 percent confidence interval, 0.2 to 0.8; P=0.02). Interestingly, the number of people that were dependent on assistance for the instrumental activities (cooking, handling finances and medication, housekeeping, and shopping) but not the basic activities did not differ significantly between the two groups. However, 4% in the intervention group and 10% in the control group were permanently admitted to nursing homes.

One of the effects was that there were more visits to GP's and physicians from the intervention group in years 2 and 3 than in the control group (mean number of visits per month, 1.41 in year 2 and 1.27 in year 3 in the intervention group, as compared with 1.11 and 0.92 visits, respectively, in the control group; P=0.007 and P=0.001, respectively).

The cost of the intervention for each year of reduced dependence was estimated to be $6000 per person in 1995. Arguably, the cost of care at patient home or nursing home is not the only consideration as the quality of life is significantly less if the person is frail. Clearly, it can be seen from the results that a proactive approach can reduce and delay the onset of frailty.

FRAILTY ASSESSMENT

The research and subsequent paper from the I.A.N.A Task force [32] forms a cornerstone of understanding on frailty assessment (Figure 4).



I stands for primary interventions and II for secondary interventions

Figure 4: The Frailty Syndrome [32]

Abellan Van Kan et al., from the I.A.N.A Task Force states that:

"…primary interventions for older persons at risk could be established to prevent "entering" a frailty syndrome (pre-frail state) or even more, the implementation of secondary interventions could render the frailty syndrome at its initial stages reversible and prevent functional decline."[32]

There are a number of assessments that can be carried out, all of which collect various data sets, belonging to a particular domain of frailty. From Figure 5, the various factors of frailty are exposed, and each domain has to be investigated and assessments made.

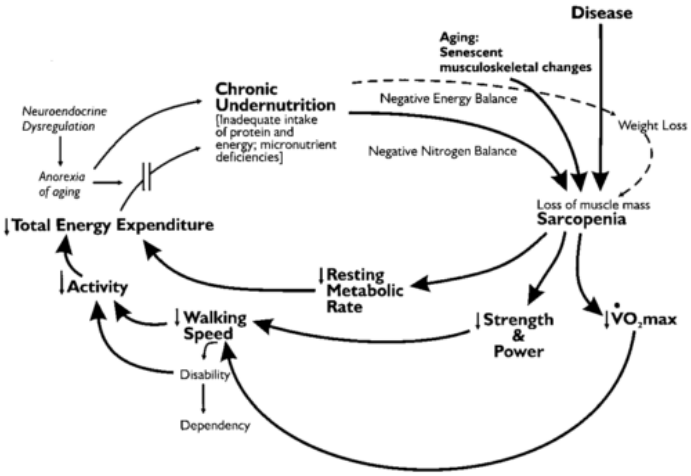


Figure 5 - Hypothesised Frailty Cycle[22]

In 2008 Xue, Q.-L. et al.[69], investigated the '*Initial Manifestations of Frailty Criteria and the Development of Frailty Phenotype…*'. This was women's health and aging observational study based over a 7.5 year period of 420 community-dwelling women with ages ranging from 70 to 79 years old. None of the women were considered to be frail at the beginning of the study (baseline); frailty was considered to be present if 3 or more of the 5 criteria had been met. The 5 frailty criteria was set as:

- Weight loss
- Slow walking
- Weakness
- Exhaustion
- Low physical activity level.

The study by Xue et al.[69] concluded that weakness was the most common first sign and that slowness and low physical activity followed with exhaustion and weight loss. However, Xue, Q.-L. et al. also stated that if the initial symptoms were exhaustion or weight loss then the risk of frailty was 3 – 5 times greater than women without any criterion.

The conclusions of the study do not directly address the risk of falls, even though the modified diagram in Figure 6 explicitly mentions it. Xue, Q.-L. (2008) et al. conclude:

'*Our findings suggest that weakness may serve as a warning sign of increasing vulnerability in early frailty development, and weight loss and exhaustion may help to identify women most at risk for rapid adverse progression.*'[69]

Chen, T.Y., Peronto, C.L. & Edwards, J.D., (2012) using 'Cognition function as a Prospective Predictor of Falls'[80] concluded that:

> '*Poor executive function (Trail Making Test), slower speed of processing (Digit Symbol Substitution [DSS] Test), and slower psychomotor speed (Digit Symbol Copy Test) were significantly associated with falls. Poor executive function and speed of processing performance (Stroop Test, Trail Making Test, and DSS Test) as well as slower psychomotor speed were significantly related to recurrent falls*' and that '*Regarding recurrent falls, being white, medication use, and balance were significant predictors.*'[80]

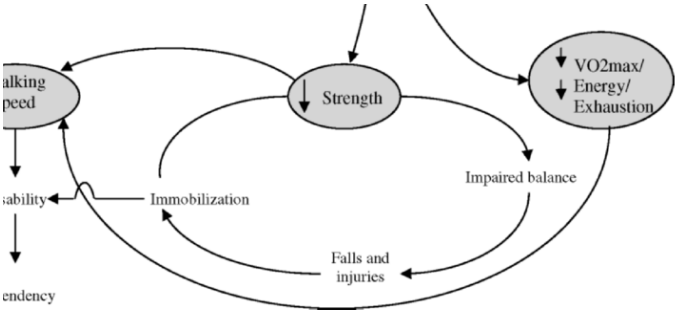


Figure 6 - Modified Frailty Cycle to include Falls [69]

PATHOPHYSIOLOGY

Clegg and Young (2011) identified the pathophysiology of frailty and described it as '*age-related changes that are fundamental to the development of frailty*'[58]. It has been argued previously that indeed the elderly are by far the most affected group; it was also shown that the affects of frailty could be experienced much earlier in life. It is considered by the author that age within itself is not a 'causal' factor, but correlates strongly with frailty as the Japanese Centurion Study[62] demonstrates by identifying positive traits for longevity which is discussed in more detail later. Strandberg & Pitkälä (2007) suggested that frailty might be as a consequence of increasing entropy and gradual disorganisation of the body [59], however, Avila-Funes et al., (2009) identifies that mental health is a good predictor of frailty.

Glymour, Tzourio & Dufouil, (2012) used the educational level of the patient and parents[71] to limited success as a predictive indicator. This could have been as a consequence of the Three City Study [66] as no base lining of the population

sample and consequently and no baseline adjustment was undertaken; bias could have also been introduced through the drop-out, death or selective participation. However, the study by Glymour, Tzourio & Dufouil, (2012) did find that parental education predicted faster decline in verbal fluency and that the patient's educational level indicated a slightly lower decline on the other tests.

Amieva, H. et al., (2014) over a 20 year period, while looking for '*Compensatory mechanisms in higher-educated subjects with Alzheimer's disease*'[72] found that:

'*The results show that the first signs of cognitive decline occurred 15 to 16 years before achieving dementia threshold in higher educated subjects whereas signs occurred at 7 years before dementia in low-educated subjects. There seemed to be two successive periods of decline in higher-educated subjects. Decline started 15 to 16 years before dementia with subtle impairment restricted to some cognitive tests and with no impact during the first 7 to 8 years on global cognition, cognitive complaints, or activities of daily living scales. Then, 7 years before dementia, global cognitive abilities begin to deteriorate, along with difficulties dealing with complex activities of daily living, the increase in self-perceived difficulties and depressive symptoms. By contrast, lower-educated subjects presented a single period of decline lasting 7 years, characterized by decline concomitantly affecting specific and more global cognitive function along with alteration in functional abilities.*'[72]

Studies have identified that Frailty is associated with a range socio-economic factors in addition to traditional bio-medical factors, such as with Linda P. Fried et al [22] who associated it with being African American, having lower education, poorer health and having higher rates of comorbid chronic diseases. This frailty phenotype was independently predictive (over 3 years) of incident falls, worsening mobility or ADL disability, hospitalisation and death. Hazard ratios ranged from 1.82 to 4.46, unadjusted, and 1.29 to 2.24, adjusted for a number of health and social characteristics predictive of a five year mortality. The research concludes two important points, that there is an intermediate stage identifying those at risk of frailty and that frailty is not synonymous with either comorbidity or disability. However, since Linda Fried published her research in 2001, more recent and subsequent studies previously discussed, Barnett et al. (2012), align multi-morbidity much more closely to the risk of frailty.

There is an on-going dialogue as to the definitions and differences of comorbidity and multi-morbidity [75,76]. Gamma & Angst (2001) found that from the same factors monitored, there was a gender difference, in that, the research was able to predict women's physical and psychological wellbeing, but the men's wellbeing did not correlate with any of the social or diagnostic variables measured[76]. Gamma and Angst concluded that women had a more holistic physical and psychological approach to wellbeing then men.

Typically educational status is not taken into account during routine evaluation, however as an additional risk factor to determine the patient's medium to long-term mental status, this could prove to be useful.

From a practical point of view, determining gradual disorganisation such as *neuroendocrine deregulation [24]* could prove a challenge and base lining could be costly; where as the *Isaacs Test* [70] or the InterRAI Community Mental Health (CMH) instrument [73] could be used to detect the onset of dementia in the elderly and determining educational status could provide insight into the likely risk trajectory.

In contrast the Japanese Centurion Study [62] concluded after investigating activities of daily living (ADLs), cognitive status, and psychosocial status that '*…autonomy in centenarians was associated with:*'

- better visual acuity
- getting regular exercise
- spontaneous awakening regularly in the morning
- preserved masticatory ability
- having no history of drinking
- having no history of severe falls after the age of 95
- more frequent intake of protein
- living at home
- and being male.

It is therefore necessary not only to recognise the negative or adverse character traits leading to frailty, but to also understand and actively promote the positive characteristics that can lead to the reduction in frailty.

Additionally to Sarcopenia, Thomas (2007)[60] and later Pepersack (2011)[61] identified Cachexia as capable of resulting in frailty. Both Sarcopenia and Cachexia have adverse muscle wasting and strength reduction outcomes. However, where as sarcopenia is a result of multiple issues outlined in Figure 6, Cachexia is a result of cancer and cannot be simply reversed or affected [61].

Clegg and Young (2011) describe the potentially sudden and dramatic decline in '*homeostatic reserve*' in those patients that are borderline dependant due to illness or minor stressor, as shown in Figure 7.

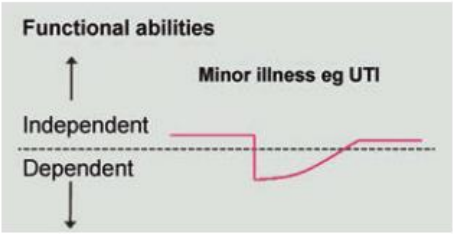


Figure 7 - Vulnerability to sudden change in health due to reduced functional reserve in frail older people [58] (UTI = urinary tract infection)

The recognition of sudden and dramatic decline that can render a patient dependant can have major implications in the functional wellbeing of the individual. The patient may have sudden weakness and reduction in strength, which may in turn create balance instability and significantly increase the risk of a fall. If minor stressors can bring on a sudden decline in homeostatic reserve, care must be taken to gradually increase physical activity and not overload the patient to early.

Quantification of the patients physical capability through an assessment such as the Groningen Activity Restriction Scale, (GARS)[77] which monitors the '*Activities of Daily Living including mobility'*, (ADL) as well as '*Instrumental Activities of Daily Living*', (IADL). The assessment is very flexible as it can be given by a carer or via email or some other electronic means.

The GARS questionnaire response categories are:

1. Yes, I can do it fully independently without any difficulty

2. Yes, I can do it fully independently but with some difficulty

3. Yes, I can do it fully independently but with great difficulty

4. No, I cannot do it fully independently; I can only do it with someone's help

GARS Question Items are:

1. Can you, fully independently, dress yourself?

2. Can you, fully independently, get in and out of bed?

3. Can you, fully independently, stand up from sitting in a chair?

4. Can you, fully independently, wash your face and hands?

5. Can you, fully independently, wash and dry your whole body?

6. Can you, fully independently, get on and off the toilet?

7. Can you, fully independently, feed yourself?

8. Can you, fully independently, get around in the house (if necessary with a cane)?

9. Can you, fully independently, go up and down the stairs?

10. Can you, fully independently, walk outdoors (if necessary with a cane)?

11. Can you, fully independently, take care of your feet and toenails?

12. Can you, fully independently, prepare breakfast or lunch?

13. Can you, fully independently, prepare dinner?

14. Can you, fully independently, do "light" household activities (for example, dusting and tidying up)?

15. Can you, fully independently, do "'heavy" household activities (for example mopping, cleaning the windows and vacuuming)?

16. Can you, fully independently, wash and iron your clothes?

17. Can you, fully independently, make the beds?

18. Can you, fully independently, do the shopping?

Gobbens, et al., 2010. Defined a new conceptual model for frailty (Figure 8). This was designed to be much more holistic than the older model (Figure 6). It would be unfair to suggest that the older model has no value, as it is still very useful in describing the relationships in the systematic decline that lead to frailty. What the older model lacks is the psychological and social elements that are seen to be important within a holistic approach to managing frailty.

The frailty assessment tools that are available have been in use for many years and currently perpetuate the '*single-disease framework*', as each tool specifically is developed to determine a specific set of parameters or performance indicators. To address the obvious requirement for multimorbibity assessment in relationship to frailty, a different approach must be taken.

From the two diagrammatic models (figures 8 and 9), we can see the contrasting approaches to developing a model to encapsulate the frailty condition. While they both have an overall holistic approach, it is necessary to understand that Gobbens, R.J.J. et al., (2010), Figure 8 favour looking at the various metrics of cognition, mental health and social aspects, where as Fried, L. P., & Walston, J. (2003) favour monitoring biomarkers.

Questionnaires

To address the multi-morbidity requirement it is useful to understand the generational nature of assessment and evaluation. The assessment or evaluation (questions to answer) of a patient for a particular condition or ailment might look very similar to a variety of other assessments and questionnaires for other diseases.

First Generation. Historically, each assessment was standalone and in 1965 Barthel et al. functionally evaluated an Index designed to measure a single construct for a single purpose. This is considered the *"First Generation"* of assessment as used in the Barthel Index for Activities of Daily Living[39].

Second Generation. The *"Second Generation"* were multidimensional instruments that addressed many clinical domains with applicability in many domains. This is an attempt to consolidate and provide an efficient assessment tool, however, these tools were specific to controlled environments such as hospitals. A common assessment tool of this generation in 1979 is the

Clifton Assessment Procedures for the Elderly (CAPE)[40]. Work on CAPE began in a few years earlier[41] in 1975; and later Pattie (1981) developed '*A survey version of the Clifton Assessment Procedures for the Elderly*'[74].

Third Generation. InterRAI (RAI – Resident Assessment Instrument) are considered to be the *"Third Generation"*[42] of assessment and provide a suite of Instruments[43], that are designed to assess an extremely broad range of clinical conditions in many settings. The assessment instruments range from Acute Care (AC) to Assisted Living and include Child and Youth Mental Health, Community Health, DeafBlind, Home Care (HC) and Long-Term Care Facilities (LTFC). InterRAI Acute Care Minimum Data Set was introduced in 2006 based on older research[44] carried out by John P. Hirdes et al., in 2001 and was tailored to assess frail hospitalised older persons. In 2008 the InterRAI assessment suite was assessed for reliability[45], 782 paired assessments across 12 nations were completed within 72 hours of each other. The resulting kappa mean value for 161 items that were common to two or more instruments was 0.75. The kappa mean value for specialised items ranged from 0.63 to 0.73 and over 60% of the items scored greater than 0.70.

NEXT GENERATION QUESTIONAIRES

Specifically, to address the '*single-disease framework*' issue highlighted previously, it is necessary to develop the concept of an 'adaptive frailty questionnaire'. This can be achieved by utilising the already existing interRAI instruments, which include:

- Acute Care
- Assisted Living
- Child and Youth Intellectual/Dev Disability
- Child and Youth Mental Health
- Community Health Assessment
- Community Mental Health
- Contact Assessment
- Deafblind
- Emergency Screener
- Home Care
- Intellectual Disability
- Long-Term Care Facilities
- Mental Health for Correctional Facilities
- Mental Health for In-Patient Psychiatry
- Palliative Care
- Post-Acute Care
- Quality of Life
- Wellness

The InterRAI Acute Care (AC) instrument is provided as a reference in Appendix 6.1. The AC questionnaire demonstrates the multidimensional nature of the interRAI approach. Within the AC sections it should be possible to determine thresholds around which 'dynamic triggers' can be set depending on the severity or predetermined criterion being met.

Once a threshold or trigger condition has been met, then depending on the section, other instruments within the interRAI suite of questionnaires can be used to enhance and augment the base set to provide greater insight into the patient's condition automatically.

There have been recent systematic reviews of frailty screening tools in primary care Pialoux, T., Goyard, J. & Lesourd, B., (2012) [8], as previously discussed. The paper concluded that SHARE and the Tilburg Frailty Indicator were suitable. While this is undoubtedly true for just identifying the onset or risk of frailty, nether one has the domain range or correlation capability (with other instruments) that the interRAI suite does, which is necessary to develop a '*dynamic approach*' to patient evaluation.

DEFICIT ACCUMULATION

This method of assessment by Kenneth Rockwood and Arnold Mitnitski (2007)[33] is particularly useful when considering multimorbidity. Rickwood & Mitnitski considered the work of Benjamin Gompertz that asserted '*the risk of death increases geometrically with age*'[81].

Figure 10 estimates that the probability of dying i.e. mortality rate, increases exponentially after approximately 20 years of age. The Gompertz Law was later modified to be subsequently known as the Gompertz-Makeham Law of mortality. The Law states that death rate is the sum of an age-dependant component (Gompertz) and an age-independent component (Makeham).

In an environment where external causes of death are uncommon or rare (low mortality countries for example), the age-independent component is usually negligible and the equation simplified into the Gompertz law of mortality.

CONCLUSIONS

From the ONS and demographic information it can be observed that there is an imperative to foster solutions that can a) monitor and b) manage the growing population of elderly. The accelerating demographic shifts in the elderly population within Scotland over and above that of Europe generally and England specifically is a wake-up call for the health can social care services. The cost burden if left unchecked and unmanaged will quickly saturate the limited dedicated budgets for the management of the elderly and eat into the core services as additional funds are found to manage the evolving problem.

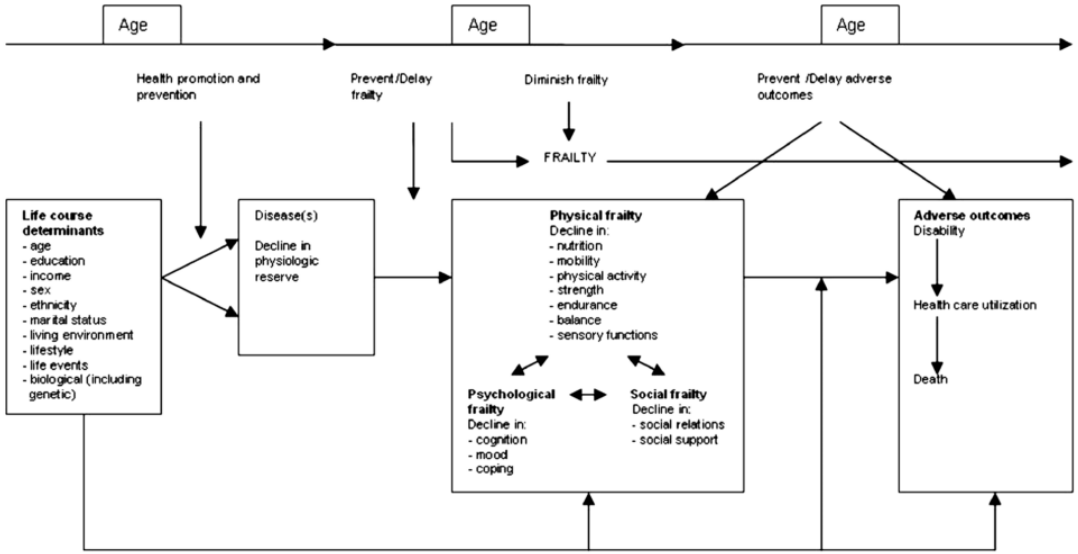


Figure 8 - An Integral conceptual model of frailty [78]

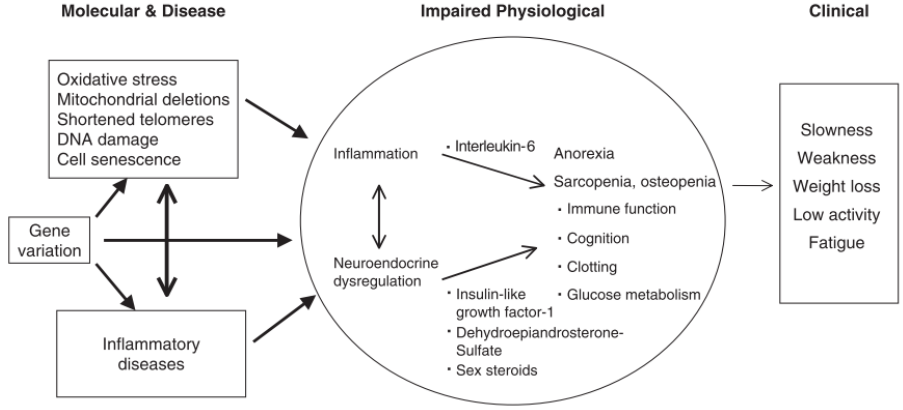


Figure 9 - Overview of Hypothesized molecular, physiological, and clinical pathway to frailty. [34]

It is possible however, to determine opportunities that lend themselves for both the monitoring and management of the frail elderly, and in addition can be applied specifically to the potential identification of a falls risk and falls prevention.

One of the novel opportunities in researching the elderly that are '*borderline dependant*', we can test for indicators of sudden homeostatic decline through over exertion or other fall metrics such as being on medication. Additionally, utilising the interRAI scoring mechanism and utilising pre-determined thresholds as triggering mechanisms, an adaptive questionnaire could be implemented. As InterRAI has a number of instruments (questionnaires), starting all patients off answering the Acute Care instrument would allow a good baseline from which to gauge future and subsequent decline. If that decline is evident than in the specific area or domain of decline other interRAI instruments can be used to gather more detailed information on the emerging condition automatically.

Clearly, from the research evidence it is possible to conclude a number of opportunities for further research and development, which could include:

- Identifying prolonged, sudden or exerted activity in a patient at risk might be a precursor to preventing falls, due to the rapid decline in homeostatic reserve. This could be achieved by monitoring of patient movement through simple wrist worn movement sensors, which could provide greater insight and diagnostic capability into identifying onset of rapid homeostatic decline.
- Multimorbidity could with further investigation provide an insight into identifying various groupings of illness that when combined together, have a higher adverse risk of frailty.
- Mental health, depression and dementia have a significant and pronounced effect on an individual with regard to frailty, more care should be exercised in determining the underlying stressors so that a more accurate assessment can be ascertained.

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